VOL. XXX TORONTO, MAY, 1934 No. 5

ANNUAL MEETING
Canadian Medical Association
June 18 to 22, 1934
ANNOUNCEMENT ON PAGE 557
CALGARY

The Canadian Medical Association Journal

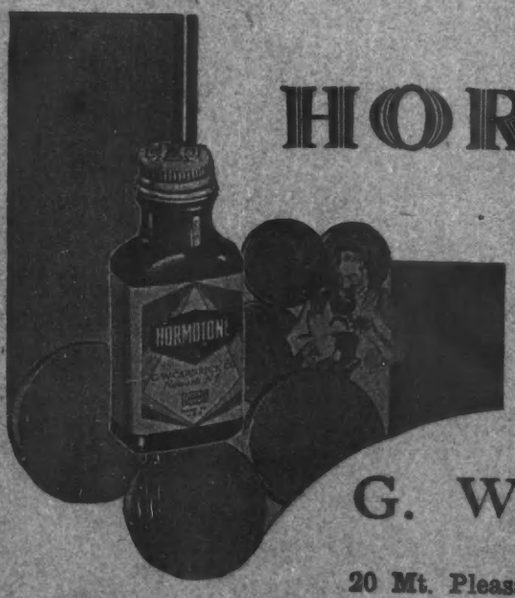
THE OFFICIAL ORGAN OF
THE CANADIAN MEDICAL ASSOCIATION
AND ITS AFFILIATED PROVINCIAL MEDICAL ASSOCIATIONS

PUBLISHED MONTHLY BY
THE CANADIAN MEDICAL ASSOCIATION
3640 UNIVERSITY STREET, MONTREAL

[PRICE SEVENTY-FIVE CENTS PER COPY]

An Endocrine Prescription in Dysmenorrhea *and* Amenorrhea

YOU can write an endocrine prescription in one word—a proper combination of the endocrine principles which are now known to initiate and control the menstrual process. Your prescription will have the advantage of being filled with fresh potent endocrine constituents. The formula is in accord with the most recent research on the endocrine glands concerned in regulating menstruation.



HORMOTONE

•

BOTTLES OF 100 TABLETS

•

G. W. CARNRICK CO.
LIMITED

20 Mt. Pleasant Ave., Newark, N. J., U. S. A.

The Canadian
Medical Association Journal

Vol. XXX TORONTO, MAY, 1934 No. 5

THE CHEMICAL NATURE OF THE FAT-SOLUBLE VITAMIN OF GROWTH—PHYTOL, CAROTIN, VITAMIN A

BY M. JAVILLIER,

Professor at the Sorbonne and at the Conservatoire National des Arts et Métiérs,

Paris, France

WHILE the idea that vitamins like the anti-beriberi and anti-scorbutus vitamins exist in certain natural media was developed by medical observation, the conception of the existence of a fat-soluble vitamin governing growth in animal organisms was derived from purely physiological studies. The first clear view seems to have been held by Stepp. This writer showed in 1909 that mice may live on a diet composed of bread made from flour and milk. If the bread were previously treated with alcohol and ether, fatty substances being thus dissolved out, the mixture became incapable of maintaining life. By combining the bread thus exhausted with the residue remaining after evaporation of the alcohol and ether employed for exhausting the bread a sufficient diet was produced.

Further developments followed in 1913, the experiments by McCollum and Davis, Osborne and Mendel. If a definite diet be formed of a protein, such as well-purified casein, carbohydrates, such as lactose and dextrin, with a little cellulose to give volume, and a suitable saline mixture, such a diet will not promote normal growth in rats. After a few weeks, the rat, showing a subnormal growth-curve, will cease to grow, will rapidly become emaciated, and will present a special lesion of the eye known as xerophthalmia. The diet employed, however, contains no fat. It must be supplemented with various fatty substances, such as lard, olive oil or butter. Experience has shown that, weight for weight, these different fatty substances have not the same food value. The diet will prove to be specially improved by adding butter; it may also be completed by adding to it an ether extract of egg yolk or liver. Certain fatty substances thus contain, and certain natural media yield, on extraction with solvents of fats, a certain substance which is active in small quantities and absolutely necessary in order that growth may occur in young animal organisms.

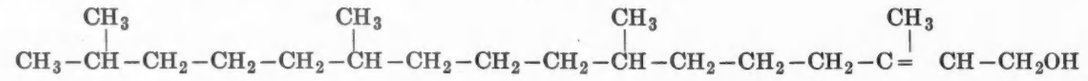
Under these circumstances originated the conception of a fat-soluble accessory factor of the diet. It proved desirable to designate this factor by the letter A in order to distinguish it from another accessory factor, soluble in water, and designated as Factor B. Here it is not necessary to show how several nutritional factors were separated later from certain fatty substances, since this discussion is limited to the factor discovered initially and constituting a growth factor and an antixerophthalmic factor. Now, what is the chemical nature of this Factor A?

Until the conditions governing the stability of Factor A to heat were defined, the factor could be considered a diastase (Drummond, 1919). This hypothesis did not prove tenable on account of the resistance of the factor to heat in the absence of oxygen. There is only a historical interest in reviewing the search for its identity among mineral substances, organometallic or metalloid compounds, fatty substances like lecithin, sphingomyelin or phrenosin, or the sterols and, especially, the phytosterols. Studies with chlorophyllic pigments were more interesting. It is very clear why the studies took this direction, for they were connected with certain facts which were observed. It was noted that alcoholic or acetonic extracts of green leaves also complete diets deficient in vitamin A. Thus

2 to 3 parts per 1000 of an alcoholic extract of *Urtica dioica*, when added to the mixture of definite and purified substances used for the experimental diet of rats, amply suffice to insure their normal growth. Again, these leaf-extracts, when treated with a cold or hot alcoholic solution of soda, air being excluded, yield after extraction with ether a water-soluble fraction containing, among other things, soaps and an ether-soluble fraction containing everything present which is designated as "unsaponifiable." The latter consists of a complicated mixture of alcohols, most of which are of high molecular weight and derived from saponification of chlorophyl and waxes, of phytosterol, of coloured carbides including carotin, and still other substances, such as xanthophyl, derived from the pigment just mentioned. Vitaminic activity proves to reside in the ether-soluble fraction. A few parts per ten thousand of this unsaponifiable residue largely suffice to obviate abnormalities due to deficiency in vitamin A, when added to the food or, better still, when administered independently of the food. The same thing occurs when an active fatty substance, such as cod liver oil or butter, is saponified. The active fraction is included with the unsaponifiable portion. From these facts, shown by the work of McCollum and Davis, Steenbock and his associates, Coward and Drummond, and myself and my collaborators, have been derived the various experiments dealing with the unsaponifiable portion obtained as indicated above. Since I was requested to discuss in this paper the fat-soluble growth factor with reference to my own studies on the subject, I may neglect many facts naturally applicable in a review, such as those shown by the patient and systematic studies by Drummond on the unsaponifiable fraction of cod liver oil.

Let us return to the unsaponifiable portion of leaf-extracts. In this fraction obtained from *Urtica dioica*, having the appearance of a waxy, reddish-yellow mass, I examined phytol in 1923 from the viewpoint of vitaminic activity, for the following reason. This unsaponifiable fraction contains many substances indicated above, such as alcohols, sterols, carbides, etc. Of these various substances, it appeared probable that the sterols and pigments had no vitaminic activity. Experiments like those of von Euler with certain sterols, and those of Drummond with carotin, were negative respecting vitamins and suggested another line of thought.

I noticed that the presence of chlorophyl often coincides with vitaminic activity. This association is not constant and certain vegetable structures which are not green have high vitaminic activity. However, the question was of interest whether phytol was the active substance or might be related to it. Phytol occurs, as we know, as an ester in the chlorophyl molecule. Chlorophyl is a methyl-phytyl-chlorophyllide. Little is known of the rôle of phytol in the chlorophyl molecule. In 1923, only its formula $C_{20}H_{40}O$ was known, and the attributed structural formula was not correct. This later was established in 1928 by Gottwalt Fischer. It appears below.



Phytol thus appears as a primary alcohol of a long aliphatic chain, linked with four CH_3 groups and having an ethylenic function. With the aid of P. Baude a phytol has been prepared in my laboratory,* by the Willstätter technique. Baude, myself and Lévy-Lajeunesse have tested this phytol with animals on food deficient in vitamin A. This phytol, well purified and tested by the so-called curative method, did not prove active. The growth curves of animals used as controls were identical with the curves of those treated with phytol, the animals dying after about the same lapse of time. The idea that chlorophyl contained something (which could be only phytol) constituting a vitamin was thus proved erroneous.

Experiment had revealed another fact before the result just stated was reached. The phytol had a certain degree of activity when not fully purified and when still slightly yellow in colour. When fed with the incompletely purified product the animals presented a temporary arrest in the declining weight and survived for a very appreciable period. For example, the control animals died in 40 days, while the treated animals lived for 60 days. If opinion had not been consolidated at this time (1924) that pure carotin is inactive (Drummond), our tests might

* Laboratory of Physiological Chemistry of the Scientific Society of Alimentary Hygiene and of the Institute of Agronomic Research.

have been interpreted as showing that our unpurified phytol owed its activity to contamination with carotin. This interpretation, however, was not acceptable, and also for another reason. By purely physical methods we decolorized the total unsaponifiable residues and found at least once, in one sample, a vitaminic activity which was slight yet still appreciable. It was clear that vitaminic activity did not depend necessarily upon a pigment. With the desire to limit ourselves strictly to the tests in mind, we noted only the "remarkable tenacity with which Factor A remains associated with carotin."

Since then, working with L. Emerique, I have divided the unsaponifiable portion obtained by a lipoidal extract of Urtica leaves into fractions containing various principles, consisting of sterols, at least one alcohol of high molecular weight, and other substances not identified, retaining only uncoloured substances. This work was discontinued when our attention was attracted by pigments present in the unsaponifiable fraction and by the possibility that they were associated with vitaminic activity. The situation in this respect had the following status. The conception that there is a certain relation between the activity of vitamin A and pigments of the carotinoid group originated with the American biochemist Steenbock. With his associates, he showed, from 1919 to 1921, that activity due to vitamin A, proved physiologically, very often coincides, in vegetable substances, with pigmentation due to carotinoid pigments. The yellow carrot and yellow maize are thus active, while colourless potato and white maize are inactive. Still further, Steenbock and his colleagues showed that carotin, of constant melting point, permits rats to resume growth suspended by omitting vitamin A from their food. However, these writers do not conclude categorically that pigment and vitamin are identical; Steenbock notes facts not fully agreeing with his earlier ideas. The correlation between pigmentation and vitaminic activity is often lacking in extracts of various vegetable substances and in substances of animal origin, Steenbock finally concluding that vitaminic activity and carotinoid pigmentation are merely coincidental.

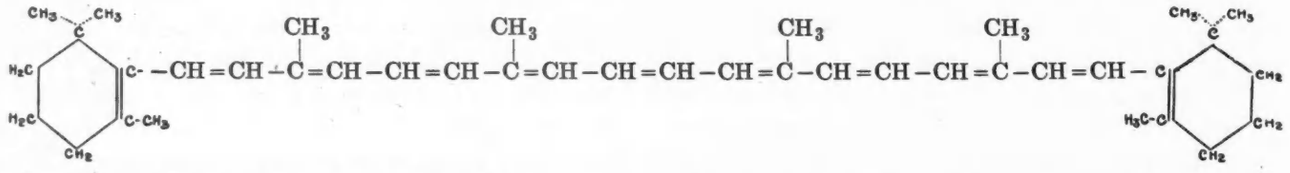
Here I do not wish to mention facts and writers in detail, presenting only the development of present ideas on this subject. I may, however, recall the fact that Drummond observed (1919) that unpurified carotin has a slight degree of vitaminic activity, and that pure and crystallized carotin is wholly inactive. This writer returned to the question of the inactivity of carotin in 1925. Facts supplied by other workers indicated that there is no common relation between vitaminic activity and the content of tissues in lipochromes. In 1923, the Japanese chemists Takahashi and Kawakami isolated an uncoloured yet active substance. As mentioned above, we conducted studies which left in suspense the question whether the vitamin was a coloured or uncoloured principle, while according with the idea that the vitamin is an uncoloured substance closely associated with a pigment.

It was the work of H. von Euler, of Stockholm, which suggested determination of the vitaminic activity of carotin. This work is based on the fact that bovine serum may notably affect growth. In seeking the active substance present in the serum, von Euler isolated carotin from it and proved that carotin has a sure vitaminic activity. Collaborating with Karrer, of Zürich, von Euler worked with carotins of increasing purity, finding in them vitaminic activity appreciable in rats to the hundredth part of a milligram and upwards (1929).

It would be of interest to show why purifying carotin without weakening its physiological properties is difficult, to indicate the experimental arrangements required for this purpose, and to show how the process of purification is followed. We are obliged to omit many points of interest to technicians, but not to an extent obscuring the progress in the development of ideas and conclusions.

Pure carotin proved to be active, an idea which failed to agree with that supported by Drummond as late as 1930. While Drummond persisted in assigning the activity observed in connection with carotin to some impurity present, others, like Collison and Moore, claimed that carotin possessed in itself the activity known as "vitaminic". When the publications by von Euler and Karrer appeared, I undertook studies, collaborating with L. Emerique, on carotin derived from unsaponifiable residues obtained from green leaves and carrots. In 1930 we announced (1), that carotin which is crystallized, but not fully pure, is physiologically active; (2), that carotin prepared 40 years before and preserved under suitable conditions remains active; and

(3), that carotin when very highly purified by our personal method still retains its vitaminic properties. We thus confirmed precisely the facts published by von Euler and Karrer, our



confirmation settling the debate between opposing opinions.

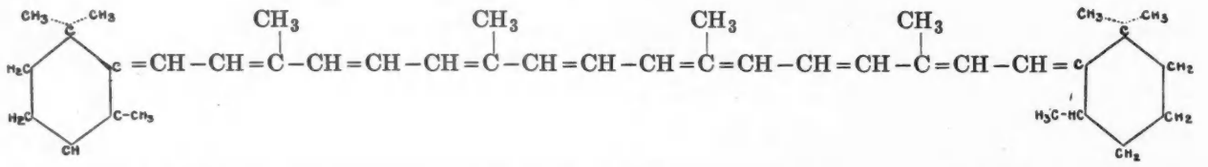
By a fortunate circumstance, Drummond discovered at the same time why his results were discordant with those obtained by others. He employed ethyl oleate for preparing his solutions of carotin, the oleate proving to act as an oxydizing catalyzer of carotin, thus rapidly inactivating the latter. In impure solutions of carotin some impurity may act to oppose oxidation, permitting the product thus to remain more or less active. By using the ethyl-lauric ester or hydrogenated cotton-seed oil instead of the ethyl-oleate ester, the vitaminic activity of carotin is not impaired and may be manifested. The fundamental point has thus been agreed upon. When a young animal is nourished with food containing no vitamin A but receives pure carotin in an oily solution by mouth, for example, no sign of avitaminosis appears. The growth curve is normal, carotin behaving like vitamin A. This idea was rendered still more certain by Van Stolk, Guilbert, Pénau and Simonnet, in 1931, who worked with chemically pure carotin, melting at 192° C. on the Maquenne block.

Meanwhile, P. Karrer, von Euler and their associates, on the one hand, and Kuhn and Lederer, on the other, showed that the term carotin includes two isomers, carotin alpha and carotin beta, which differ in their melting points, position of absorption bands, and optic activity. Both isomers act as vitamin A with practically equal intensity. Here intervene the important contributions by Karrer and his collaborators, who showed the structure of the carotin molecule. Discussion on this point would involve purely chemical considerations, not opportune in this *Journal*. Only the conclusions need be given.

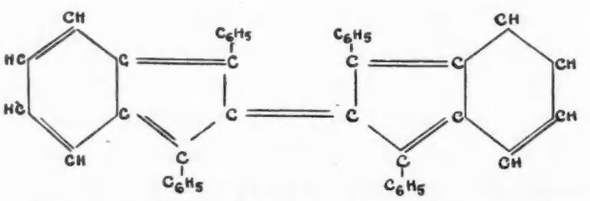
Beta carotin may be represented as follows:

It is carotin without rotatory activity. There is no asymmetrical atom of carbon in its formula. It has two identical cyclical chains, exists in beta-ionone, a well-known odorant substance, and possesses between its two cycles a long, unsaturated chain with nine double connections arranged symmetrically.

Alpha carotin appears to correspond to the following formula, whose differences with that of beta carotin readily appear on fairly close examination:



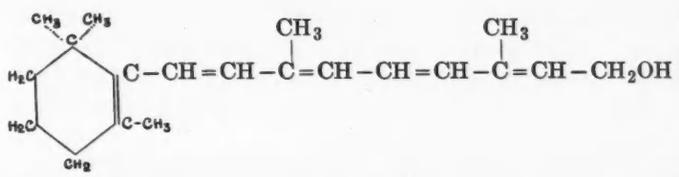
I may recall the fact that I had meanwhile shown, with Emerique, that another hydrogen carbide has no property relating it with vitamin A when it is ingested. This other product is very interesting. Its colour is a superb orange-red, it has many double connections and is decolourized by fixing oxygen. It is rubrin, an artificial carbide, $C_{42}H_{28}$, its structural formula being quite different from that of carotin (Ch. Moureu, Ch. Dufraisse and P. M. Dean), as follows:



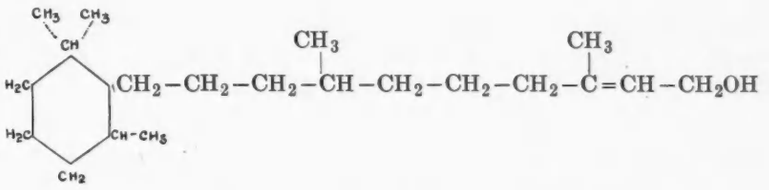
The vitaminic activity of carotin was thus firmly established, so firmly, in fact, that carotin was selected to serve as the international standard for vitamin A at the London conference on the standardization of vitamins. In spite of this fact, carotin does not seem to be the only active substance of the kind. Some of the points mentioned at the outset of this paper indicate this clearly. Other facts in

point also exist. Among natural products cod liver oil is especially rich in vitamin A. The activity of the oil is evidently not due to carotin, or to carotin alone. The colour of the oil is not that of a simple solution of carotin, nor is this colour in relation with its activity. Some highly-coloured oils have little activity, as I pointed out in 1923, with P. Baude. The intensity of the reaction between cod liver oil and stibic chloride in a chloroform solution (the Carr and Price reaction), more or less accepted as a reaction of vitamin A, differs frankly from that occurring when this reagent is applied to carotin. T. Moore has shown in a remarkable way the characters differentiating carotin from the active substances of cod liver oil. The hepatic vitamin does not have the same absorption spectrum as that presented by carotin. Moore states that the hepatic vitamin is uncoloured and not a pigment. He also inquires what becomes of carotin when ingested, showing that it is stored, especially in the liver, in quantities which may be considerable and also in other organs, such as the kidney and lung. It is not stored in the form of the coloured substance carotin, but as an uncoloured substance, being transformed either in the liver or in the blood.

The physical methods applied by Bruins, Overhoff and Wolff indicated that the molecule of this uncoloured substance is smaller than that of carotin. The carotin molecule is therefore split by the storage process. This is a remarkable fact, for the storage of physiological principles is usually accomplished by molecular condensation. Glucose, for example, $C_6H_{12}O_6$, is condensed in the liver in the form of glycogen, $(C_6H_{10}O_5)n$. The correctness of this experimental deduction was soon brilliantly confirmed. P. Karrer and his associates have extracted the active substance of the hepatic oils of two fishes, the hyppoglosse and the scombresoce, and give its structural formula, with some reserve, as follows:



This formula shows that the active substance of the liver, $C_{20}H_{30}O$, represents half a molecule of carotin, having an alcoholic function at the end of its long lateral chain. Here we find phytol, which we studied seven years ago. The relation between phytol and vitamin A is shown by comparing their two general formulas (phytol: $C_{20}H_{40}O$ and vitamin A: $C_{20}H_{30}O$) and, especially, the structural formulas which are assigned to them. Comparison is rendered particularly easy by expressing phytol as follows:



In short, vitamin A consists merely of phytol, dehydrogenated and provided with a cyclic structure, as I have pointed out.

This is by no means all. The vitaminic activity of the active hepatic substance is greater than that of carotin. The quantity of carotin sufficing to permit resumption of growth in a rat weighing about 100 grams, and whose growth curve is rendered stationary by deficiency in vitamin A, is 0.002 mg. The corresponding quantity of the active hepatic substance is, according to von Euler and P. Karrer, about 0.0003 mg. Carotin is thus split, stored, and has its vitaminic activity multiplied.

In view of its very high activity, it seems reasonable to consider the active substance of the liver as vitamin A and limit this term to it. But here arises the question of naming carotin. It is not a pro-vitamin, for were it such, it would be incapable of acting by itself and could act only after transformation into a vitamin *in vivo*. It rather acts by itself, behaving merely as a less active vitamin A. Discussion on this point is only of academic interest.

We have presented the relations of composition and structure allying carotin, vitamin A and phytol. Plants contain both carotin and phytol. But do plants also contain vitamin A in type like the hepatic vitamin, that is, a non-pigmentary substance corresponding to one-half the carotin molecule and acting as a growth factor?

An affirmative reply is favoured by the fact that I have observed uncoloured leaf extracts having a certain activity in promoting growth. Kellström, a pupil of von Euler, has found in leaves of the barley plant a substance giving the spectrum of vitamin A. It seems very probable that vitamin A exists in plants not only as a pro-vitamin but as a true vitamin in the sense defined above.

What is the relation of phytol to these data? It does not act as a growth factor when ingested. From the time of my work with P. Baude, however (1925), it has appeared to me that phytol might be related to vitamin A "with respect to origin or composition." I have just now related how correct was this view. Facts known for a long time thus admirably agree with facts newly discovered.

1. Pigmentation due to carotinoid substances present in various materials is not directly proportional to the vitaminic activity of these materials, since not every carotinoid substance acts as an agent of growth.

2. Carotin and the raw material containing it are active, either because carotin has vitaminic activity in itself or because it is transformed into an active substance *in vivo*. At all events, carotin when ingested produces the effect assigned to vitamin A.

3. The vitamin present in the livers of fish is an alcohol whose molecular weight corresponds to one-half the molecule of carotin. It has no colour and there is no longer any reason for expecting that natural substances of vegetable or animal origin should not possess the activity characteristic of vitamin A, even if these substances be not coloured with carotinoid derivatives.

4. There is an evident relation of composition and structure existing not only between carotin and vitamin A but also between the active vitamin and the inactive phytol.

There is small need to stress the importance of these points in their applications to physiology and medicine. The fat-soluble growth vitamin is of the first importance during the entire growth-period of the organism. It is doubtless less necessary quantitatively in adults, but it is really needed by adults as well as by children, since it also combats infection. Vitamin A cures hikan and experimental xerophthalmia in whatever form it is provided. It increases resistance to pneumonia, and several striking results obtained with it in puerperal fever have been published. Von Euler and Gard have recently shown that it acts against the bacterium causing pasteurellosis in the rat. Carotin, or raw material containing an abundance of it, has been tested in experimental tuberculosis. We have also made a few insufficient tests of it in this field, but it has nowhere given any very distinct results.

It is of great importance to ascertain the process through which vitamin A acts. Utilizing the idea that vitamin A seems to be essentially a growth factor, I have collaborated with Allaire and S. Rousseau in determining whether its absence from the diet causes any imbalance in the nucleic phosphorus present in the tissues, that is, the form of phosphorus characteristically present in cellular nuclei. Experiment showed that its absence produces no such imbalance. The proportion of nucleic phosphorus differs so little in mice fed insufficiently with the fat-soluble factor from that present in those whose diet is not deficient that the difference cannot be employed to show that vitamin A is concerned in the synthesis of the nucleic compound. If it is so concerned, proof must be provided on other grounds.

The characters of the solubility of vitamin A and of its association with fatty substances naturally suggest that its mechanism should be sought in connection with the metabolism of fats and lipoids. Working with Emerique and Rousseau, I have found that deficiency in vitamin A is accompanied by a diminution of cholesterol in the different organs, except the skin. This fact is, perhaps, not unimportant. Again, my collaborator Emerique has observed that intestinal absorption of glycerides is not affected by deficiency in vitamin A.

Recent literature presents other data in this field. Euler has reviewed them in a recent conference. Facts thus far available, however, do not permit the formation of positive teaching on the subject. It is not doubtful that the improvement made during recent years in the chemical point of view will give wings to equivalent progress in the spheres of Physiology and Physic.

THYROTOXICOSIS AND THE AUTONOMIC SYSTEM*

BY ANDRÉ CROTTI, M.D., LL.D., F.A.C.S.,

Grant Hospital,

Columbus, O., U.S.A.

THE endocrines and the autonomic system are so intimately correlated that one cannot study one without the other. These two systems are the outstanding regulating and correlating mechanisms affecting all the vegetative functions of the body. One might well ask which of the two is the more important. Such a question cannot be answered easily. One might say, however, that the endocrine system is much older than the vegetative system, because we know that in lower life there is no autonomic system; the metabolic exchanges are essentially controlled by the endocrines. Later in the animal scale the autonomic system makes its appearance, and as the animal organism becomes more and more complex the two systems assume a more profound and intimate relationship. Further, in this era of extensive sympathectomies and ganglionectomies no untoward appreciable disturbance in the general physiological behaviour of the individual has seemingly resulted, a thing which would not certainly be true if the same wholesale attacks were to be made on the endocrines.

For these two reasons one might regard the endocrines as playing fundamentally a more essential part in the endocrine-autonomic mechanism, the autonomic playing largely the part of a marvellously efficient and quick transmitter of impulses. Naturally, these two systems are meant to be in perfect functional balance. If, however, one of the two should become functionally or organically disturbed it will at once repercuss not only upon the other system but also upon the whole physiological behaviour of the organism. Further, we shall have to remember that the physiological equilibrium in the vegetative structures is largely dependent upon the colloidal structure of the cells and their relative content of the various ions. With this in mind, it is easily understood that a given cellular structure might respond in a different way to a given hormone or to given nerve impulse, the response being dependent upon its intimate physical, chemical and electrical cellular structure. We see at once, consequently, that the stability of the whole neuro-endocrine mechanism is a delicate and an easily vulnerable one. For that reason, a person with a hypersensitive autonomic system will respond to stimuli which in a normal one will pass unnoticed. The same is true of the endocrine system, which becomes "geared up" to produce more sympatheticotropic hormones than parasympatheticotropic ones, and *vice versa,* thus producing an imbalance between the two divisions of the autonomic.

It is generally conceded that the nerve control from the autonomic system reduces itself to two fundamental functions — stimulation and inhibition, and it is, further, generally conceded that the endocrine hormones act upon the nervous system either centrally or peripherally. Thus, it becomes obvious that these two systems are closely interlinked.

Hormone control is much slower and much less efficient than that produced by the nervous system. For example, secretin, produced by the duodenal glands when stimulated by the acid content of the stomach, passes at first into the blood circulation, and goes through most of the organisms before it centres its hormonic effect upon the pancreas and liver, thus causing a flow of pancreatic juice as well as bile. It apparently exerts its effect upon these two organs alone, but takes a roundabout way to do so. The same is true of adrenalin, produced by the chromaffine system; it is first thrown into the blood stream, and only then centres its hormonic effect upon the sympathetic system. Thus, it becomes apparent that our organism would be much handicapped for quick transmission of impulses if it were to rely upon the endocrines alone. Production, transmission and diffusibility of impulses would be too slow, especially in case of an emergency. It needs a quick transmission mechanism, hence, the autonomic. To be sure, the auto-

* Read by invitation before the Ontario Medical Society, Hamilton, Ont., on June 2, 1933.

nomic is not only a passive transmitter, passing along impulses born elsewhere, but it is capable of originating impulses of its own.

The autonomic system is divided into two structurally distinguishable divisions: 1st, the sympathetic; 2nd, the parasympathetic.

The sympathetic originates from that portion of the spinal cord extending from the first thoracic to the 4th lumbar segment. That is why it is sometimes called the thoraco-lumbar system. As the organism ascended in the animal scale and became more and more complex, the motor neurones and the sympathetic system wandered out of the cord, forming the sympathetic chain composed of ganglia connected by fibres; this is known as the ganglionated cord, extending from the atlas to the coccyx. These ganglia, however, retained their intimate relationship to the cord by connecting fibres, the white rami communicantes, transmitting efferent impulses, and the grey rami communicantes transmitting afferent impulses.

The ganglia forming the chain along the vertebral column are known as the vertebral ganglia. There are also numerous others located farther in front of the vertebræ and known as the prevertebral or collateral ganglia, and finally there are some others lying in the musculature of the viscera and termed terminal ganglia. Sympathetic ganglia are masses of nerve cells which form the motor neurones of the sympathetic system. They are really relay stations serving as distributing centres of impulses. The reflex centres of the sympathetic are located in the lateral horn of the gray matter.

The parasympathetic originates from the midbrain and from the sacral portion of the cord. That is why it is sometimes called the cranio-sacral division of the autonomic. The parasympathetic fibres, as a rule, do not pass through the lateral ganglia as the sympathetic ones do, but run from the brain centres directly to the organs themselves. There are, however, a few exceptions. For example, the fibres destined to form the vagus run first through the ganglion jugulare and the ganglion nodosum and only then form the vagus nerve. Both systems, the sympathetic as well as the parasympathetic, contain stimulating as well as inhibiting fibres.

Sympathetic stimulation results in the following: dilation of the pupils, protrusion of the eyeballs, lessened lacrimal secretion, dry mucous membrane of the nose and throat, hypoacidity, hypomotility and hyposecretion of the gastro-intestinal tract, general relaxation of the intestinal musculature leading to a certain amount of gastro-intestinal dilatation, rapid pulse, vasoconstriction of the peripheral blood vessels and slight rise in blood pressure, hyperglycæmia, diminution of the urinary output, increased sweating, increased body-heat, increased metabolism.

Parasympathetic stimulation gives the following reactions: contracted pupils, increased Dalrymple and Von Graefe, increased lacrimation, increased naso-laryngeal secretion, increased salivation, laryngo-spasm, increased bronchial secretion with bronchial spasm, slowing of the heart, vasodilatation, lowering of the blood pressure, hypersecretion, hypermotility of the gastro-intestinal tract, irritable bladder with spasm of the neck of the bladder, sweating and diminished body-heat, lowered metabolism. From this it is quite apparent that these two systems appear to be antagonistic; what one stimulates the other inhibits, and *vice versa.*

As most of the vegetative structures are supplied by both sympathetic and parasympathetic, it becomes apparent that a normal physiological equilibrium is maintained by a happy antagonism of the two divisions of the autonomic system. This mutually antagonistic arrangement is devised for the purpose of maintaining a physiological balance in the organs, one system acting as a check upon the other. This protective check is indeed essential, because without it abnormal stimuli might lead to disastrous consequences. Consider, for instance, what a very high fever might do to a heart were there no autonomic system. Ordinarily, each organ possesses a considerable degree of reserve force which will prevent the physiological equilibrium from being disturbed; in other words, prevent symptoms from appearing. It is only when the functional tonus as well as rhythm is interfered with unduly long, or with undue intensity, that the physiological balance is disturbed. Thus we may conclude that the physiological equilibrium is maintained by the antagonism of the two sets of fibres, the sympathetic and the parasympathetic.

The study of the reactions of the autonomic system to the various pharmacological products has served much to throw light upon this com-

plex subject. For instance, the intravenous injection of adrenalin produces the same results as does electrical stimulation of the sympathetic, hence, the conclusion that adrenalin activates the sympathetic. The adrenal glands may be consequently regarded as the pharmacodynamic centres of the sympathetic. On the other hand, it has been found that pilocarpine does to the parasympathetic what adrenalin does to the sympathetic: it reproduces the symptoms obtained by stimulation of the parasympathetic. Hence, the conclusion again that pilocarpine is an activator of the latter division of the autonomic. Pituitrin, too, is regarded as a parasympathetic stimulant.

Cushing has recently published some highly interesting observations concerning the action of pituitrin and pilocarpine. Pituitrin, injected intramuscularly or intravenously, causes a marked vaso-constriction, translated by blanching of the skin and mucous membranes, causes a dryness of the mouth due to suppression of salivary secretion, produces an antidiuretic effect, and finally induces a prompt bowel evacuation due to stimulation of the lower bowel, which is a parasympathetic effect, the other reactions obtained being those of sympathetic stimulation.

Injected intraventricularly, pituitrin calls forth a totally different response. It produces: (1) an intense flushing of the skin due to vasodilatation; (2) profuse perspiration; (3) marked salivation and lacrimation; (4) retching and vomiting, intestinal hypermotility; (5) a fall in body temperature; (6) a lowering of basal metabolism; (7) oliguria. Injections were made in the lateral ventricles in patients operated upon for pituitary adenomas.

Two possibilities arise as to the way in which the extract works. First, resorption into the blood stream; this is improbable if we remember the way pituitrin acts when injected intravenously—causing vaso-constriction instead of vasodilatation, etc. Second, direct stimulation of the hypothalamic nuclei, the pituitrin diffusing through the ependymal cells lining the third ventricle. This supposition is the most likely one, because we know that electrical stimulation of the tuber cinereum increases the active principle of the posterior hypophysis.

In conclusion, pituitrin injected into the lateral ventricle produces parasympathetic stimulation, apparently of hypothalamic origin. Further, as the neuro-hypophysis is seemingly under the direct control of the tuber cinereum; it would appear that its physiological product, pituitrin, passes directly into the field of the ventricular cavities, and thence goes to stimulate the parasympathetic centres in the subthalamic region.

Pilocarpine acts in the same way as does pituitrin when injected into the ventricular cavities.

Just how and where drugs act upon the organs is not fully understood. They are supposed to stimulate the autonomic endings in the glands and the myoneural junction of the smooth muscles. How can we explain that pituitrin, used intravenously or intramuscularly, gives totally different reactions than when given intraventricularly? There must be reasons, but what they are are not known. If it is true that sweating, salivation, lacrimation, retching and vomiting, vaso-dilatation, fall of basal metabolism and body heat, caused by the intraventricular injection of pituitrin represent a parasympathetic discharge very similar to the sympathetic discharge induced by adrenalin, then it is logical to look upon the posterior pituitary as the activator of the parasympathetic in the same manner as the adrenals are regarded to be the activator of the sympathetic.

The thyroid receives its nerve supply from both the sympathetic and the parasympathetic. The sympathetic connector fibres arise in the upper thoracic segment of the cord, go to the third cervical ganglion, and supply the blood vessels as well as the secretory cells of the thyroid. After connecting a galvanometer with the thyroid gland and the neighbouring tissues, Cannon observed that stimulation of the sympathetic high in the thorax produced an electrical current, while stimulation of the vagus caused no such current. Clamping of the blood vessels supplying the thyroid did not cause any electrical changes. He therefore concluded that the sympathetic fibres of the thyroid gland may be reasonably assumed to be true secretory nerves. At the same time he observed that stimulation of the adrenals to increased activity causes a characteristic reaction of the thyroid. In experimenting on the cat, the anterior root of the right phrenic nerve was fused with the right cervical sympathetic, thus causing a volley of nerve impulses to the thyroid each time the

animal breathed. In four of the animals which survived operation, symptoms and metabolic changes very similar to those in exophthalmic goitre in man were observed. All symptoms receded after resection of the right half of the thyroid was performed, hence, Cannon's conclusion that the thyroid is subject to that division of the nervous system which causes adrenal secretion. This conclusion is based upon the claim that during emotional excitement the adrenals are stimulated into production of greater quantities of substances which liberate sugar in the urine, cause abolition of the muscular fatigue, dilatation of the bronchioles, inhibition of digestion, and redistribution of the blood in the body, with rapid coagulation.

Rogers, Fawcett and Beebe, in 1914, and Watts, in 1915, showed that stimulation of the cervical sympathetic caused a diminution of the iodine content in the thyroid. Cannon and Cattell, in 1916, and Cannon and Smith, in 1921, showed that the sympathetic is a vaso-constrictor of the thyroid vessels and an excito-secretory agent of the thyroid gland. They further observed that sympathetic stimulation reduced the iodine content of the gland. Cannon, in 1922, found that the introduction of an extremely slight amount of adrenalin into the blood stream will cause marked acceleration of the denervated heart. The same result is obtained if the afferent nerve to the adrenal gland is stimulated. Simple massage of the thyroid gland produces acceleration of the denervated heart, even when the adrenal gland has been previously removed. Likewise stimulation of the cervical sympathetic will produce the same effect, by increasing the output of thyroxin in the blood stream. Thus, he claims that the thyroid is under the control of the sympathetic system. Hammet, in 1923, experimenting upon albino rats, found that thyro-parathyroidectomy caused a great retardation in the growth of the central nervous system, and that the brain is more dependent upon the thyroid function for its proper growth and differentiation than is the cord. Hicks, in 1926, and Hektoen, Carlson and Schulhof, in 1927, found that stimulation of the sympathetic would produce an increased output of iodothyreoglobulin in the thyroid venous blood. Mason, Markowitz and Mann, in 1930, claimed that the thyroid has no secretory nerve, but that the sympathetic acts as a vasoconstrictor.

Physiologically speaking, there seems to be a discrepancy in the claim that the sympathetic acts as a vasoconstrictor of the thyroid vessels and at the same time as an excito-secretory agent of the thyroid. It is strange, indeed, to observe a vaso-constriction in the face of an excito-secretion; ordinarily, increased physiological secretion means increased blood supply. Be that as it may, one cannot but accept the view that the sympathetic must have some influence upon the physiology of the thyroid.

The parasympathetic fibres destined to the thyroid come from the superior and inferior laryngeal as well as from a branch originating from the vagus. According to Ascher-Flack, in 1910, the electrical irritation of the peripheral end of the superior laryngeal nerve produces an increased secretion of the thyroid, and Frank and Hallion have demonstrated that it is vaso-dilatatory. The central irritation of the depressor nerve causes an intense vascularization of the thyroid through a reflex intermediary action of the external laryngeal nerve. Hence, the superior laryngeal nerve seems to be vaso-dilatatory as well as excito-secretory.

The thyroid, the adrenals, the parathyroids, and the genital glands seem to be controlled by the sympathetic, whereas the pancreas, the posterior pituitary, thymus and secretin-producing glands seem to be under the influence of the parasympathetic. In thyrotoxicosis we have largely a mixed picture of sympathetic and parasympathetic stimulation. In the majority of patients sympathetic stimulation is the dominant one. In few cases, however, the picture is clearly of parasympathetic stimulation. There is no case in which one division of the autonomic is stimulated to the exclusion of the other.

In 1910, Eppinger and Hess sought to explain the thyrotoxic syndrome on the basis of sympatheticotonia and vagotonia. As criteria of their vagotonic condition, beside the various clinical signs observed, they tried to show that these patients were naturally hypersensitive to pilocarpine and relatively refractory to sympathetic stimuli and epinephrine injections. Hence, their claim that these patients showed a natural imbalance in favour of the parasympathetic; they are vagotonic. In sympathetic cases the patients were naturally sensitive to adrenalin injections and reacted by an increased clinical syndrome induced by the goitre, such as exophthalmos, high blood pressure, tachycardia, atonic condition of

the bowel, gastric hypoacidity, dryness of the skin and mouth; hence again, their conclusion that such patients were naturally hypersensitive to adrenalin. They are sympatheticotonic.

Their distinction between these two entities was most likely too closely drawn. This grouping, however, is of great clinical importance, as it classifies the reaction tendencies of those belonging to either system. Indeed, there is no question that some persons seem to have a preponderance of sympathetic tendencies; others, of parasympathetic. Some other persons may have only a definite set of organs unduly sensitive to one of the two systems, and, again, some others may show a combination of sympathetic and vagotonic symptoms; for instance, a truly vagotonic patient may have a rapid heart action, or some other symptoms of sympatheticotonia.

These apparent inconsistencies might be explained by the very condition of the cell itself; its chemico-physico-electrolytic state will largely determine its behaviour and its reaction. They might become less puzzling, too, if we knew better the intricate mechanism of innervation of the tissues. Further, we have seen that hormones may be sympatheticotropic or parasympatheticotropic; for instance, adrenalin is a powerful sympatheticotropic agent, the pancreas markedly vagotonic; the thyroid is both sympatheticotropic and parasympatheticotropic. And, finally, the reciprocal influence of the various endocrines one upon another, as well as upon the autonomic, must be taken into consideration. When all is said and done, the picture of hyperthyroidism is certainly a mixed one; one in which the thyroid is stimulated, one in which the autonomic is stimulated, and one of polyglandular reciprocal hypo- and hyper-functioning influence. The conclusion I reached in my book, "Thyroid and Thymus", in the first edition in 1918, seems to still hold good, that hyperthyroidism is a thyro-neuro-polyglandular disease.

Exophthalmos in connection with thyrotoxicosis is quite frequent. Seldom does it assume such proportions as to lead to the extrusion of the eyeballs and blindness. It ordinarily recedes more or less after thyroidectomy. Progressive exophthalmos after thyroidectomy, though not common, has been and still is the most baffling problem confronting the goitre physician and surgeon. It is frequently the only mark of the disease that once existed. Its characteristic is to be progressive, leading sometimes to almost complete extrusion of the eyeballs and total blindness. The etiology in both instances must be the same. What the real cause can be is still much debated. Of late, a great deal of attention has been paid to the congestion taking place in the orbital structures such as the orbital muscles, fat, etc. A brief description of the following case will serve to illustrate what happens in such instances.

A man about 58 years old presented himself with an almost complete extrusion of the right eye, panophthalmia, loss of vitreous, total blindness in that eye. The left eye was not protruding, no Dalrymple, no Graefe, present; the eyesight was apparently normal. The thyroid was about five or six times the normal size, not unduly vascular, firm, of the thyrotoxic type; of the diffuse parenchymatous variety. The patient had been quite nervous, complained of palpitation, loss of flesh, etc. Metabolism was plus 33. The first clinical diagnosis was of thyrotoxicosis. The unusual feature of the case was the extreme unilateral exophthalmos. Such an extreme case I have never before encountered.

The eye was enucleated first, and ten days after a thyroidectomy was performed.

In performing the enucleation care was taken to inspect the muscles and the retro-ocular fat, and specimens of both were removed for microscopical examination. Macroscopically, the orbital muscles were found to be enormously hypertrophied, to at least ten times the normal size, and the retro-orbital fat was swollen and dense. The histological findings in the eye muscles showed various degrees of œdema, fibrosis, and cellular infiltration. Most of the muscular striations had disappeared; interstitial œdema was quite marked; fibrous degeneration, varying in degree, was obvious in many places. Lymphocytic infiltration, especially around the blood vessels was present. The retro-ocular fat showed distinct signs of fibrous organization.

The same findings have been found by various authors. This being the case, the explanation of exophthalmos becomes simply a mechanical one. Indeed, the orbital space is a pyramid widely opened outside and sharply pointed inside. The walls of the pyramid, however, being completely bony are totally unelastic; any pressure from without must of necessity push the orbital content outside. Thus it becomes obvious that if the orbital muscles and orbital fat become so unduly hypertrophied as to occupy most of the orbital space the globus oculi must necessarily protrude; there is no other possibility.

On the strength of this, some may say that the mechanical explanation of exophthalmos becomes quite clear, but in no way does it explain the *why* of the changes that do take place in the orbital content. The answer to this enigma might possibly be found in a dis-

turbed function of the autonomic system. These trophic disturbances observed in the orbital structures might well be regarded as of autonomic origin, and I might cite quite a few arguments that militate in favour of this point of view.

We must bear in mind that nutrition of the tissues depends upon the nerve and blood supply. Nutrition and function of the body cells are inseparable. Consequently, disturbances of the blood supply and innervation of a given region must be followed necessarily by trophic changes, since the nutritional requirements of the cells are profoundly disturbed. Striated muscles, as shown by Dusser de Barenne, are supplied with sympathetic fibres. Neuron disturbances may also be responsible for some of these trophic changes; thus injuries to neurons may induce excessive stimulation or inhibition, resulting finally in regional metabolic disturbances. One can easily understand that an organism whose nerve endings receive stimuli greater than normal over a long period of time would end by manifesting nutritional changes in the organ concerned.

Further, if we understood fully the mechanism that leads to production of œdema we might perhaps have a clearer insight into what happens in the orbital structures under discussion. For instance, œdema in a limb where thrombophlebitis has occurred has been interpreted as being due to the mechanical impairment of the return flow on account of the venous obstruction. However, Ranvier proved that aseptic ligature of the femoral vein and of the inferior vena cava does not induce œdema, providing no infection occurs. Consequently, the mechanical obstruction alone is not the sole cause of the œdema; there must be some other intervening factor.

Already in 1871, Ranvier, after ligating the vena cava below the renal vein and after severing the sciatic nerve, observed an œdema on the same side, providing the division of the nerve was done just below the point where the vasomotor fibres join the sciatic nerve. If the section was made above, no œdema occurred. Leriche and Young have obtained the same results; hence, the conclusion that the vasomotor system plays a great part in the production of œdema. Leriche has shown that when the venous segment involved by the thrombophlebitis is excised the œdema disappears. How can we explain this? Most likely it is because the thrombosed segment is transmitting vasoconstrictory impulses in the segment below the thrombosis through its perivascular sympathetic. Perhaps, too, the reason is because the sympathetic controls directly the vasosecretory power of the vascular endothelium, thus disturbing the equilibrium of the serous exchanges. That the œdema may take place and disappear exceedingly rapidly and must be under autonomic control is shown by these cases of sudden and segmentary œdema which occur in certain regions of the body, such as the lips, cheeks, hands and feet, appear almost instantaneously, and after a while disappear in the same manner. I have observed a young woman whose upper lip swelled considerably under my very eyes, the swelling subsiding altogether within about twenty minutes. She had had this same experience several times before. There was no apparent cause for it. How could this occur if there were no nervous control? Remember also those two cases of severe œdema of the hand and arm, one observed by Leriche and the other by Brandao. In these two cases œdema disappeared at once on the operating table as soon as sympathectomy was done. This proves that œdema is largely under autonomic control. In view of all this, the orbital trophic disturbances observed in progressive exophthalmos could perhaps be explained on the basis of autonomic control.

What part the sympathetic and what part the parasympathetic play, if any, should bear further investigation. I fully realize that cervical sympathectomies performed in some of these cases did not give the results hoped for. This should by no means be regarded as final; perhaps, a closer study of the autonomic innervation of the orbital structures might afford some useful information.

With this point of view in mind, namely, that progressive exophthalmos might be due to a viscero-trophic reaction of sympathetic origin, a patient who presented a marked progressive exophthalmos was treated with *acecoline*.*

He had marked puffiness of the eyelids, conjunctival œdema and lacrimation. The exophthalmometer showed: rt. 27 mm.; left, 28 mm. at 100. He complained of some aching, especially on movement. Upward movements of the globus oculi were much impaired; the

* This is a French preparation having much the same properties as acetylcholine. [ED.]

downward lateral movements less so; the optic disc was œdematous.

Acecoline was chosen because it was regarded as a parasympathetic stimulant. If, perchance, the progressive exophthalmos was due to the viscerotrophic reaction of sympathetic origin, it was thought that acecoline by stimulating the parasympathetic would bring about a restoration of the physiological equilibrium between the two systems of the autonomic, and thus benefit the patient. A full ampoule was given daily for 25 days.

Some improvement was obtained; rt. eye 27½; left, 27¼ at 100. After cessation of the injections the exophthalmos resumed its progressive course. At the present time it is quite marked and the vision is much interfered with. There seems to be only another course open, namely, orbital decompression, as advocated by Naffziger.

Another patient with progressive exophthalmos, a woman, was given fifty daily injections of acecoline without much results.

In the face of these and other negative results one should not become discouraged, because, after all, orbital decompression, though the only course open in extreme cases, does not strike at the cause, but relieves only the results of the cause still unknown. We must find the cause.

THE ETIOLOGY OF UNDULANT FEVER IN CANADA: *BRUCELLA ABORTUS* ISOLATED FROM TWO CASES IN QUEBEC*

BY REDVERS THOMPSON,

Macdonald College, McGill University,

SINCE the first report of a case of undulant fever in Canada in 1928, an increasing interest in Brucella infection by public health authorities, medical practitioners and veterinarians has been evident. While cases of undulant fever have occurred sporadically in various sections of Canada, little bacteriological work on the disease has been carried out, the diagnosis having been based on agglutination tests and on clinical symptoms, neither of which are sufficient to directly incriminate any one member of the Brucella group as the etiological factor. The studies of Evans[1] have shown the marked similarity of the three types of Brucella organisms—*Br. melitensis,* whose natural habitat is the goat; *Br. suis,* whose natural habitat is the hog; and *Br. abortus,* the organism associated with infectious abortion in cattle. The *melitensis* and *suis* varieties of Brucella have been generally accepted as pathogenic for man, but there is still some question concerning the *abortus* variety.

Bevan[1] of Rhodesia, in 1921, first called attention to cases of undulant fever probably related to cattle infected with contagious abortion. He reported that out of the first 35 cases studied, 84 per cent were in males. Otero[2] has successfully inoculated three persons by applying *Br. abortus* to the abraded skin. Thompson[2] reported that 94 per cent of 64 veterinarians engaged in rural practice in Denmark showed the presence of agglutinins for Brucella organisms in their blood. Of 18 senior veterinary students, 15 reacted positively five months after leaving school and entering practice. Poppe,[2] on the other hand, tested 29 veterinarians in Germany and found them all negative.

Smith[2] considers that the abortus variety is only slightly pathogenic for the human subject—or perhaps pathogenic under unusual circumstances. Carpenter and King[2] present evidence to show that the abortus strain from milk is only slightly pathogenic for man. Orr and Huddleson[2] show that in the United States only 1.5 per cent of people constantly exposed to the abortus organism through an infected milk supply showed evidence of infection with the organism.

Hardy[1] concludes that both the *abortus* and *suis* varieties are about equally responsible for the undulant fever morbidity in Iowa. The incrimination of any one member as the etiological factor of undulant fever in United States has been made more difficult because of the prevalence of goats, and because of the known frequency of Brucella infection in hogs. Taylor and Hazemann[3] have shown that the abortus variety is the etiological factor in a small percentage of cases of undulant fever in France. Gilles and Peres,[4] however, report 3 cases of undulant fever in France of bovine origin, but which were shown to be infected with the *melitensis* strain. The organism isolated from the milk supply was the *melitensis* and not the *abortus* variety. Kristensen[2] concludes that in Denmark 30 to 40 per cent of the cases of undulant fever are caused by drinking milk contaminated with the *abortus* variety. Contact with cattle played an important rôle, while swine did not appear to be the source of infection in any of the cases.

From the evidence presented, it is evident that there are wide variances of opinion regarding the pathogenicity of *Br. abortus* for the human being. The problem has been retarded because of the fact, first, that in countries where the etiology of undulant fever has been studied infection of goats and swine was known to be present, and, secondly, even though evidence pointed to a contaminated milk supply, it is possible that the cattle were infected with the *melitensis* or the *suis* varieties. Extensive comparative bacteriological studies must be carried

* Received for publication on February 28, 1934.

out concurrently on cases of undulant fever and on the suspected milk supply before the question can be satisfactorily answered.

While it appears that *Br. abortus* is not extremely pathogenic for the human family, yet, we do not know whether this organism is just beginning to adapt itself to man, or whether undulant fever has not been recognized until recently; in my opinion, both factors have been operating. In this connection, Hall has recently stated that "undulant fever prevalence may be on the up-curve, potentially at least. If nothing is done to control the disease a great epidemic wave of this ailment among men, in the not far distant future, is a catastrophe which is well within the realm of the possible."

BRUCELLA INFECTION IN CANADA

Since few goats are maintained for milking purposes in Canada, it would seem that infection with the *melitensis* strain is unlikely. To accept such a hypothesis as fact in view of the present knowledge, however, would be unscientific. Information on the presence of Brucella infection in hogs indicates that the *suis* variety is not likely to be the etiological agent in the undulant fever of this country.

Gwatkin[2] reports the presence of agglutinins for Brucella in low dilutions in 0.6 per cent of 500 hogs studied at a Toronto abattoir. On the other hand, investigations carried out by the Health of Animals Branch show that Dr. E. A. Bruce was unable to demonstrate agglutinins for Brucella in several thousand samples of hogs' blood collected in British Columbia, and that Dr. L. Heath also had negative results on samples of hogs' blood collected in Alberta. Investigations carried out at the Ontario Veterinary College also demonstrate a low incidence of porcine infection in Canada.

That infectious abortion in dairy cattle is widespread in Canada is evidenced by reports from veterinarians and farmers from every province. Watson,[5] Chief of the Pathological Division of the Dominion Health of Animals Branch, relying on data compiled from results of serological tests carried out two years ago, shows that there was 20 per cent infection in the herds examined. No statistics are available to show the relative infection in the various provinces. Dr. R. L. Conklin, Director of the Veterinary Service of the Province of Quebec, presents figures to indicate at least 12 per cent infection in the province.

Dr. R. A. McIntosh, of the Ontario Veterinary College, from serological tests conducted in Ontario, estimates that 20 per cent of the dairy cattle harbour Brucella organisms. In extensive bacteriological investigations on milk from animals reacting to the blood test, Thompson[6] has shown that all Brucella organisms isolated were of the *abortus* variety. So far as the author is aware, not once has either a *melitensis* or *suis* strain been isolated from milk or from dairy products in Canada. It has been shown by Gwatkin[7] and also by Thompson[8] that *Br. abortus* is eliminated with the milk of a high percentage of cattle reacting to the blood test in dilutions of 1:100 or higher, and it has further been demonstrated by Thompson[9] that the organisms are transmissible to butter and to ice cream and are viable in these products for periods longer than the normal storage time.

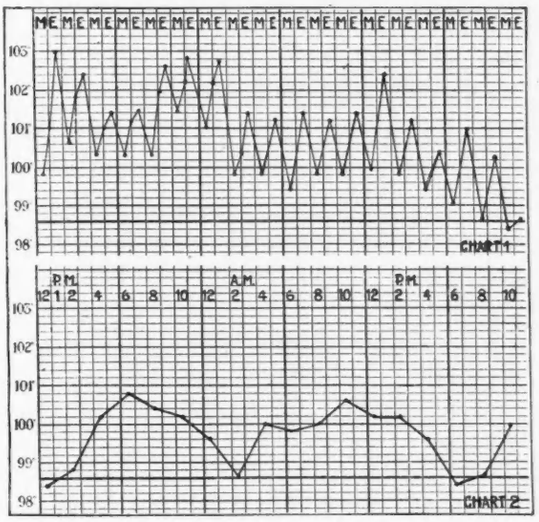
In view of the above knowledge, frequent transmission of *Br. abortus* to the human would seem inevitable. According to the presented information, it would seem logical to assume that the cases of undulant fever reported in Canada by Harris,[10] McLean,[10] Warner,[10] Hannah,[11] McKay,[14] Stalker,[12] Murray,[12] Wesley,[13] McIntyre,[12] Hill[15] and Hardman,[16] have been caused by infection with the abortus variety, either by direct contact with infected animals or through the drinking of infected milk, or the eating of infected dairy products. Since, however, from none of these reported cases has an organism been isolated which exhibited the characteristics of *Br. abortus* in the requirements for increased carbon dioxide, any statement pertaining to the etiology of the disease in Canada must be based upon very limited information.

It is of interest to note that the mortality rate from undulant fever in Canada, is somewhat higher than that reported from other countries. Hardy[1] reports a case fatality rate of 3 per cent in his cases in Iowa. Starr[2] reports a mortality rate of about 1 per cent from cases studied in Virginia. Taylor and Hazeman[17] report that in France the mortality rate is about 3 per cent. Hardman,[16] from data based on 225 cases in Ontario, reports a case fatality rate of 6.6 per cent. Considering the circumstantial evidence of the incrimination, and at the same time the considered low pathogenicity of *Br. abortus*, this becomes a perplex-

ing question. The above figures are, of course, based on limited evidence, and much further investigation is necessary before any accurate estimation of mortality rates in Canada can be given. The increasing incidence of undulant fever in Quebec is causing much concern to Public Health Authorities. In this connection the following case reports with the bacteriological findings are of interest.

CASE 1

P.C., male, aged 45 years, gave an agglutination titre to *Br. abortus* of 1:200. This patient was admitted to hospital on December 7, 1933, but had complained of a general weakness and tired feeling for a period of five weeks previously. During his sojourn in hospital no regular temperature charts were kept, but readings taken at irregular intervals showed a wide variation. Within six-hour periods there was a temperature fluctuation of 4 degrees F. The highest temperature fluctuations continued for a period of five days. On December 17th, 10 c.c. of blood were drawn from the patient and were cultured on fresh liver infusion agar by a technique which had been found by the author well adapted to the isolation of *Br. abortus* from milk. Duplicate cultures were made, one incubated in an atmosphere containing 10 per cent carbon dioxide, and the other ærobically. All cultures were incubated at 37° C. After fifteen days' incubation the cultures incubated in the carbon-dioxide-rich atmosphere revealed typical colonies of *Br. abortus*, while the plates incubated ærobically failed to produce growth. Microscopic, cultural and serological tests corroborated the colony characteristics.



The patient did not drink milk, but used raw cream freely on cereal. The cream supply was obtained from a herd of fifteen cows, five of which were reactors to the agglutination test for *Br. abortus* in dilutions of 1:160 or higher. *Br. abortus* was isolated from individual animals and also from the mixed milk and from the cream. A comparison of the two organisms showed a marked similarity in CO_2 requirements and in colony appearance, the only difference observed was in the rapidity of growth in the original isolation, the organism from the blood of the patient requiring 15 days and the organism from the milk requiring only 5 days for the production of typical colonies.

CASE 2

S.L., female, aged 59 years, gave an agglutination titre to *Br. abortus* 1:640. This patient had complained of feeling tired and listless for a period of three weeks previous to the onset of increased temperatures. She was not admitted to a hospital, but had the services of a trained nurse. The temperature charts reproduced here show the fluctuations. Chart I represents oral readings taken at 9 a.m. and at 6 p.m. from the date of the onset of fever, January 22nd, until February 8th. Chart II shows the fluctuations at two hour intervals on February 20th and 21st.

The patient drank milk from a herd composed of 5 cows, one of which was shown by agglutination test to be infected with *Brucella* organisms. On February 9th fifteen cubic centimetres of blood from the patient and milk samples from individual quarters of each animal in the herd were cultured. After twelve days' incubation in an atmosphere containing 10 per cent CO_2, the cultures from the patient's blood revealed the presence of *Br. abortus;* the organism has not to date, however, been isolated from the milk supply.

Blood from two other cases diagnosed clinically and serologically as undulant fever has been cultured, but in each case has failed, by the methods employed, to reveal organisms belonging to the Brucella group. *Br. abortus* was isolated from the milk supply used by one of these patients.

SUMMARY

1. A brief summary of the historical aspects of *Br. abortus* in relation to undulant fever is outlined.

2. *Br. abortus* has been isolated from the blood of persons, in Canada, showing clinical symptoms of undulant fever.

The author wishes to acknowledge the cooperation of Dr. E. A. Foley, of the Provincial Bureau of Public Health, for information pertaining to outbreaks of undulant fever, and to express his thanks to Dr. H. Deschambault and Dr. H. LeBlanc for helpful assistance.

REFERENCES

1. National Institute of Health, Bull. 158, Iowa, 1930.
2. Virginia Agr. Exp. State Tech. Bull., 1933, vol. 48.
3. TAYLOR, R. M. AND HAZEMAN, R. H., *Rev. d'Hyg.*, 1932, **54:** 520.
4. GILLES, M. AND PERES, G., *Rev. Gen. de Méd. Veterinaire*, 1932, **41:** 476.
5. WATSON, E. A., personal communication, Feb., 1934.
6. THOMPSON, R. R., Ph.D. thesis, McGill Univ., Oct., 1932.
7. GWATKIN, R., Report Pub. Health Ass. Meeting, Toronto, 1933.
8. THOMPSON, R. R., *J. Inf. Dis.* (in print).
9. THOMPSON, R. R., *Canad. M. Ass. J.*, 1932, **29:** 9.
10. *Pub. Health J.*, 1928, **19:** 272, 274, 314.
11. HANNAH, *Canad. M. Ass. J.*, 1929, **20:** 396.
12. *Canad. M. Ass. J.*, 1930, **23:** 62, 247, 677.
13. WESLEY, *idem.*, 1930, **22:** 676.
14. MCKAY, *Canad. Pub. Health J.*, 1929, **20:** 85.
15. HILL, *Canad. M. Ass. J.*, 1932, **26:** 449.
16. HARDMAN, *Canad. Pub. Health J.*, 1933, **24:** 347.
17. TAYLOR, R. M. AND HAZEMAN, R. H., *Rev. d'Hyg.*, 1932, **54:** 519.

THE CLINICAL APPLICATION OF HÆMATOLOGY TO INFANTS AND CHILDREN*

BY CHARLES E. SNELLING, M.B. AND ALAN BROWN, M. D., F.R.C.P.(C.),

Toronto

HÆMATOLOGY in this discussion will include cytology, pigment metabolism, and the physical properties of the formed elements of the blood. Many of the blood examinations carried out in ward laboratories are done as a routine and are frequently considered in that light. The following example will illustrate the meaning. A clinician was asked by a student for the routine used in his hospital in the treatment of a certain disease. He replied, "We have no routine, because routines make one cease to think. Here we treat patients, not diseases, and certain procedures are carried out as the indication arises." It is the purpose of this paper to illustrate the value of many of the laboratory procedures done on blood.

The following include most types of examination: Erythrocyte count, leucocyte count, platelets, hæmoglobin estimation, smear, differential count, the appearance of the cells, their size, vital staining with cresyl blue, oxydase stain, supravital staining, hæmatocrite, sedimentation, grouping, Van den Bergh test, icteric index, fragility, urobilin, bile test, (see 1, 2, 3, 4 and 5 for methods). Before the results can be evaluated the normal values must be known. These are shown in Tables I, II, and III. Table I is taken from Blackfan, Baty and Diamond[6] and gives the normal values for the various elements of the blood. Table II is taken from Blackfan and Diamond[7] — "The monocyte in active tuberculosis". Table III gives the normal values for many of the properties of the blood and pigment metabolism.

The examination of the blood is diagnostic in certain conditions. Anæmias have as the outstanding laboratory feature lowered hæmoglobin. There are many types of anæmia in

* From the Wards and Laboratories of the Hospital for Sick Children, and the Department of Pædiatrics, University of Toronto, under the direction of Alan Brown.

TABLE I.
NORMAL VALUES

Age:	*At birth*	*2 days*	*5 days*	*10th day*	*2 wks.*	*6 mos.*	*1 yr.*	*2 yrs.*	*4 yrs.*	*8–12 yrs.*
Red blood cells (M)....	6.22	5.8	5.8	5.5	5.3	4.9	5.0	5.0	5.0	5.0
Hgb. (percentage)	130	132	120	110	100	80	80	85	90	90
White blood cells (T)..	15	23	11	11	11	10	10	9	8	8
Platelets (T)	400	300	300	300	300	300	300	300	300	300
Polymorphonuclears	45	55	40	35	35	40	40	40	50	60
Eosinophiles and basophiles	3	5	5	4	4	3	2	2	2	2
Monocytes	12	15	12	10	6	6	5	8	8	8
Lymphocytes	30	20	40	50	55	51	53	50	40	30
Premat. white blood cells	10	5	3	1	0	0	0	0	0	0
Nucl. red blood cells....	++	+	+	0	0	0	0	0	0	0
Reticulocytes (percentage)	1	3	1.5	1	0.5	0.5	1	1	1	1

TABLE II.
MONO-LYMPHOCYTIC RATIO
Estimated Normal.

Age	*W.B.C.*	*—Mono—* *Percentage*	*Total*	*—Lympho—* *Percentage*	*Total*	*M:L*	*Ratio*
0–6 mos.	12,000	5	600	50	600	1:10	0.10
6 mos.–1 yr. ...	11,000	6	660	44	4,840	1:7.3	0.14
1–4 yrs.	9,000	8	720	32	2,880	1:4.0	0.25
4–12 yrs.	9,000	8	720	27	2,430	1:3.4	0.29
Adults	8,000	7	560	24	1,920	1:3.4	0.29

TABLE III.

NORMAL VALUES

(a) The oxidase stain[8]

Positive	*Negative*
Polymorphonuclear neutrophiles	Basophiles
Polymorphonuclear eosinophiles	Lymphocytes
Myelocytes	Clasmatocytes
Monocytes	Myeloblasts

(b) Diameter of red blood cell—7.7 microns, average.
(c) Hematocrite in infants—43-60 per cent.
(d) Sedimentation rate—0.08-0.35 per minute.
(e) Bleeding time—1-4 mins. Clotting time—2-8 mins.
(f) Clot retraction—normally in 1 to 2 hours.
(g) Capillary resistance occasionally positive.
(h) Van den Bergh, indirect, 1 to 2 units.
(i) Icteric index—up to 6.
(j) Bile—none in urine and stool (except young infants).
(k) Urobilin—very slight in urine—is the pigment of the stool.
(l) Urobilinogen is precursor of urobilin in fresh urine.
(m) Fragility begins at 0.45 per cent saline; complete in 0.34 per cent.
(n) Blood grouping — Jansky I and II common in Western races; III and IV common in Eastern races.

infancy and childhood, with findings somewhat peculiar to each. The more common are:

(a) The result of infections.
(b) Dietary.
(c) Prematurity and twin pregnancy.
(d) Primary anæmias.—
1. Erythroblastic. 2. Congenital.
3. Pernicious.
(e) Hæmolytic diseases.—
1. Acholuric jaundice. 2. Malaria.
3. Sickle cell anæmia. 4. Erythroblastosis.
(f) Chemical poisons.—
1. Lead. 2. Benzol.
(g) Secondary to primary blood dyscrasia.—
Leukæmia, thrombopenic purpura, aplastic anæmia, Hodgkin's disease.

Over 50 per cent of a series of 300 cases with anæmia collected by Blackfan, Baty and Diamond[6] were due to either acute or chronic infection. Acute infections in the young are nearly always associated with the development of anæmia, though the response of the other elements of the blood may vary even for the same type of infection. Syphilis and tuberculosis of any duration cause a decrease in hæmoglobin. The usual feature of anæmia associated with infection is the more or less parallel decrease in the red blood cells and hæmoglobin. In other words the colour index remains slightly less than unity. (Table IV).

Dietary anæmia is the preferable term for this type, as it indicates the factors bringing about the changes noted.[6] Dietary anæmia develops in infants or animals kept exclusively on a milk diet beyond the usual suckling period. It is due to the lack of iron in milk and is very quickly overcome, even in the severe cases, by the ingestion of adequate amounts of iron in an assimilable form.

TABLE IV.

	R.B.C. M	*Hgb. Percentage*	*Colour Index*	*W.B.C. T*
Infection				
1. Acute	3.8	65	0.9	2.4
2. Acute	3.4	60	0.89	28.0
3. Acute	1.1	22	1.0	28.0
4. Tuberculous	3.0	60	1.0	15.8
5. Plumbism .	3.8	62	0.82	6.3
Prematurity				
6. (9 weeks) .	2.8	52	0.93	
7. (10 weeks).	3.0	58	0.96	
8. (11 weeks).	2.8	50	0.89	
Diet + Prematurity				
9. (14 mos.)..	2.8	35	0.6	8.4
10. (10 mos.)..	4.2	60	0.7	16.4
11. (14 mos.)..	2.8	33	0.58	7.8

The hæmatological findings are low hæmoglobin. The red count may be decreased, but usually not as much as the hæmoglobin, so that there is a low colour index. On smear examination achromia, polychromasia, poikilocytosis, anisocytosis, stippling and, occasionally, nucleated red cells are found (Table IV).

Prematurely born infants invariably develop anæmia. It is considered that this is the result of a physiologically immature bone marrow, possibly due to lack of sufficient bone marrow space.[6, 10] The characteristics of anæmia of prematurity are that it is most marked usually around the tenth week, the decrease in blood count and hæmoglobin are more or less parallel, and the colour index remains near unity. Later, if poor diet enters into the picture, one finds the red count going up and the hæmoglobin still remaining low, so that many, when seen at 6 months of age or later, have a picture indistinguishable from the dietary type. One of twins, occasionally both, may have the same course as premature infants (Table IV).

Primary anæmias or anæmias where there is disturbance of the blood cell formation in the bone marrow with no assignable cause are not so rare as is usually considered. Primary pernicious anæmia (Addison-Biermer type) is very rare. Congenital anæmias[6] are fairly frequently reported, and are in infants who are born with low counts and hæmoglobin. Some of these may be a type of erythroblastosis that have not been observed until they are in a hypoplastic anæmic state.

Erythroblastic (Cooley's) anæmia[11] occurs in Greek, Italian and other Mediterranean races. The blood findings are quite typical. The red count and hæmoglobin are usually decreased to a variable degree. The colour index is low.

Leucocytosis is constant. In the smear the cells vary markedly in size and shape, and are poorly filled with hæmoglobin. Polychromasia is present in many. The immaturity of the cells is shown by many reticulocytes, Howell-Jolly bodies, Cabot rings, basophilic stippling, and the large number of nucleated red cells in various stages of development, some of which may be undergoing nuclear division. The number of nucleated erythrocytes may be very high, especially after splenectomy, when they increase in unusually large proportions. The Van den Bergh reaction is positive indirect.

TABLE V.

Case	*R.B.C. M*	*Hgb. Percentage*	*W.B.C. T*	*Corrected W.B.C. T*	*Nucleated Erythrocytes*
1. Pre-operative	2.5	21	23.4	10.8	12.6
Post-operative	5.1	75	42.0	23.0	19.0
" "	2.3	35	188.0	77.0	111.0
" "	2.2	34	192.0	73.0	119.0
" "	1.6	25	99.2	23.8	75.4
2. Pre-operative	1.7	19	28.0	22.0	4.0
" "	2.8	30	32.0	30.0	2.0
Post-operative	3.2	45	29.3	19.3	10.0
" "	3.2	50	31.0	20.0	11.0

Two sisters with erythroblastic anæmia. The smears showed a large number of normoblasts, erythroblasts and megaloblasts. Anisocytosis, poikilocytosis, polychromasia and hypochromia were marked. Platelets and leukocytes appeared normal.

The icteric index is increased. Urobilin is often present in the urine. The stool contains large quantities of urobilin. The urine is frequently quite brick red on the diapers, from urates. The fragility test is normal or has an increased span (Table V).

Very closely related to the above conditions are those in which hæmolysis is an important feature.[12] This group includes sickle cell anæmia, hæmolytic jaundice, malaria, and erythroblastosis. Sickle cell anæmia is a condition seen in the negro in which anæmia is present due to excessive breakdown of erythrocytes. The icteric index and Van den Bergh may be slightly increased. The excretion of urobilin in the stools and urine is increased. The fragility of the blood is normal. The diagnostic feature is the formation of crescentic shapes (sickling) by the red cells when standing in sealed cover-glass preparations. Latent types may be seen where the blood has the sickling tendency, but anæmia is not present.

Hæmolytic jaundice is diagnosed by the hæmatological findings.[13] Anæmia is present with lowered hæmoglobin and red cells. The counts vary from one to four million; the hæmoglobin from 20 to 60 per cent. The red cells tend to microcytosis, averaging 6 to 7 microns in diameter. Evidences of immaturity, such as polychromasia, stippling, Cabot rings, and Howell-Jolly bodies, are seen, and reticulocytes are increased, usually from 10 to 30 per cent, but have been much higher. The resistance of the red blood cells to hypotonic saline solutions is markedly diminished, so that hæmolysis begins as high as 0.75 to 0.8 per cent and is complete at 0.40 per cent. The icteric index is increased. The Van den Bergh is increased indirect. The urine contains no bile, but has urobilin. The amount of urobilin in the stool is increased as much as ten times the normal. After splenectomy the increased excretion of urobilin stops, the jaundice disappears, anæmia clears up, reticulocytes and evidences of immaturity are not found, but the fragility frequently remains increased. The acquired form has the distinguishing feature that there is usually no microcytosis, but the erythro-

TABLE VI.

THREE CASES OF HÆMOLYTIC JAUNDICE WITH PRE- AND POST-SPLENECTOMY LABORATORY FINDINGS

Case	*R.B.C.*	*Hgb. Percentage*	*Reticulocytes Percentage*	*Fragility*	*Urine Urobilin*	*Stool Urobilin*	*V. d. B. Units*	*I.I.*
Case 1								
Pre-operative	1.5	35	15	0.76-0.50	+ +	400-950	2.5	25
Post-operative	4.75	71	3.6			6.0-80	0-1.4	4-10
2 months	5.96	78	1.0					
Case 2								
Pre-operative	2.64	48	32.0	0.72-0.34	+ +	Increased	6	30
10 days post-operative	4.03	80	4.0	0.72-0.34		Normal		
14 days post-operative	3.65	68	1.0			Normal		
Case 3								
Pre-operative	2.5	45	20	0.76-0.4	+		6	
Post-operative	5.2	77	1.0	0.55-0.35			1	

cytes may tend to be somewhat larger than normal (Table VI).

Malaria is diagnosed by the finding of the plasmodium in the blood smear. There are anæmia, increased excretion of pigment, and other evidences of red cell destruction. It is of little concern in this country.

Erythroblastosis probably includes icterus gravis, hydrops fetalis, etc.[14] The blood shows a very large number of nucleated erythrocytes, increasing severe anæmia in which there is a decrease in the number of cells as well as in the hæmoglobin. The icteric index is increased. The Van den Bergh test gives a positive biphasic reaction and bile is present in the urine, though very little is found in the stools. This picture persists for some time after birth, which distinguishes it from the normal normoblastic increase seen in new-born infants, which disappears by the second or third day of life.

Lead is the chief chemical poison that affects the blood of infants and children.[15] If there is a history of pica, or if the symptoms suggest plumbism the smear will often aid in the diagnosis. There is a mild to moderate secondary anæmia with basophilic stippling as the outstanding feature. The number of stippled cells may vary from 3 to 4 per cent up to 15 to 20 per cent (Table IV).

Secondary anæmia is always present in leukæmia, thrombopenic purpura, aplastic anæmia, Hodgkin's disease and Banti's disease.

Lymphatic leukæmia[1] is more common in infants and children. It is usually acute and frequently in the aleukæmic phase. In most of the cases the red cells and hæmoglobin are decreased with a colour index approaching unity. The platelets have been invariably decreased except during remissions, and purpura is frequently seen. The total white count has varied, but in a large number is below 5,000, with from 80 to 100 per cent of the cells from the lymphoid series. Young, immature forms are found. In some the nuclei are to be seen dividing; in others the irregular Rieder forms. The cytoplasm in the younger forms is darker and frequently very scanty in amount in the stained smear. The nuclei stain irregularly, and nucleoli are unusually evident. Due to the thrombopenia the bleeding time is increased, capillary resistance is frequently positive, and clot retraction is poor. The oxidase stain of the blood smear shows that the cells are not of the myeloid series (Table VII).

Myeloid leukæmia is infrequent in children, and is usually of the chronic type. The anæmia is present to a variable degree. The white count is high — 100,000, more or less. The platelets may be decreased. Frequently in the stained smear they are seen to vary in size, some being as large as erythrocytes. The various forms of the myeloid or granular cells make up 90 to 100 per cent of the differential count. The oxydase stain is positive for most of the cells.

Monocytic leukæmia,[16] though it is rare, is recognized by the supravital examination of the blood. It is similar to the other types of leukæmia, except that the largest proportion of the white blood cells are immature monocytes.

TABLE VII.

LYMPHATIC LEUKÆMIA

Case	*R.B.C. M*	*Hgb. Percentage*	*W.B.C. T*	*Granular Cells*	*Lymphocytes*	*Remarks*
Case 1						
Dec. 17	4.4	75	5.3	30	70	Red blood cells normal. Platelets normal. Few lymphocytes—appear immature.
Jan. 29			4.5	5	95	Platelets decreased. Lymphocytes immature.
T and A						
Feb. 3			4.8	60	40	Normal smear.
Feb. 14	4.5	80	7.8	4	96	Immature cells. Platelets scarce.
Mar. 10	2.8	60	3.2	1	99	Immature cells. Platelets scarce.
Case 2						
Nov. 8	2.7	42	2.2	16	84	Platelets decreased. Lymphocytes immature.
Jan. 14			28.8	2	98	Platelets decreased. Lymphocytes very young.
Jan. 28			4.8	1	99	No platelets seen. Nearly all blast. forms.
Died						

In the supravital preparation stained with neutral red and Janus green the monocytes have salmon pink granules tending to form a rosette, and the immaturity of the cell is in proportion to the number of mitochondria which take the green stain.

The following are a group of conditions in which the laboratory examination of the blood aids in the diagnosis.

Purpuras may be of two types, thrombopenic, or unassociated with thrombopenia. In the latter the blood is not changed. The thrombopenic purpuras may be divided into two groups — the idiopathic and the symptomatic. In the latter the condition clears up with the removal of the focus of infection and repeated transfusions. Splenectomy usually alleviates the idiopathic type, though the thrombopenia often persists.

The blood findings in these are varying degrees of secondary anæmia, with the outstanding feature of lowered platelets. If the platelet count falls below 60-80,000, bleeding is extremely probable. The counts in thrombopenic purpura are from 10-40,000. The bleeding time is increased. The capillary resistance test is positive. Clot retraction does not take place after many hours. The idiopathic type continues with this picture; the symptomatic type clears up with repeated transfusions. This therapy may have to be continued for as long as three or four months at intervals, before one can decide definitely. The number of the idiopathic group is very small if the observer will have the patience to wait. Purpura is often a manifestation of leukæmia (Table VIII).

Hæmophilia shows a normal bleeding time, but the clotting time may be prolonged to days. The usual clotting time by the capillary method is 3 to 8 minutes; the venous clotting time is 10, at the outside limit. After sensitizing to protein, repeated intradermal tests with the protein bring the capillary clotting time to normal, but have no effect on the venous clotting time.[17] The capillary resistance test, platelets, and other properties of the blood are normal.

In acute active tuberculosis the blood reacts with a specific tendency.[7] The monocytes are increased, the lymphocytes decreased, and the polymorphonuclear neutrophile is increased. This has been found to be consistently true in the acute forms, such as miliary, meningeal and pneumonic, but in the less severe types, where clinical and x-ray signs suggest activity in the glands or parenchyma of the lung, possibly allergic in nature, we have been unable always to demonstrate the increase in monocytes; the polymorphonuclear neutrophiles have been increased and the lymphocytes decreased in almost every case. Coincident with improvement the lymphocytic count increases and the neutrophiles and monocytes drop. In all cases there is an associated anæmia in which both the red count and hæmo-

TABLE VIII.

PURPURAS

Case	*R.B.C. M*	*Hgb. Percentage*	*Platelets T*	*—Time— Bl. Mins.*	*Cl. Mins.*	*Remarks*
Case 1.—Jan. 3 Symptomatic infection	1.1	22	40	15	2.5	Very occasional platelets seen in smear; many normoblasts, polychromasia, and reticulocytes. Capillary resistance, positive. Clot retraction, negative.
Jan. 17	3.5	65	375.0	2.8	2.5	Platelets plentiful.
Case 2.—On admission scarlet fever				31	15	No platelets. Capillary resistance, positive. No clot retraction.
1 week later				4	3	Platelets plentiful.
Case 3.—Leukæmia			35.0	13	4.5	Very few platelets.
Case 4.—Pre-operative. Idiopathic thrombopenic	1.2	25	5.3	25	3.5	Few platelets. Capillary resistance, positive. No clot retraction.
1 month post-operative	3.0	60	19.3	6	3.5	Few platelets.
3 months post-operative	4.6	80	180.0	3	3.5	Numerous platelets.

TABLE IX.

TUBERCULOSIS

Case	W.B.C. T	Polymorphonuclears Percentage	Lymphocytes Percentage	Monocytes Percentage	M / L	Remarks
Case 1						
9 months	15.8	61	27	11	1 / 2.5	Active tuberculosis.
2 weeks later	16.2	73	15	12	0.8 / 1	Active tuberculosis.
3 months later	12.3	29	67	4	1 / 17	Marked improvement.
Case 2						
12 years	8.2	60	33	7	1 / 4.7	Tuberculous pleural effusion.
Case 3						
14 months	15.1	66	28	6	1 / 5	Moderately active lesion.
Case 4						
6 years	23.2	85	7	8	1.1 / 1	Miliary and meningeal.

globin are decreased. Supravital preparations confirm the findings of the fixed smear, and show the epithelioid cell or stimulated monocyte, which is considered as diagnostic of tuberculous activity (Table IX).

The large endothelial phagocytes, or clasmatocytes,[8] are cells which phagocyte inert material. They are not in the circulating blood normally, but where particles such as bacteria are floating in the blood stream they are frequently present in fairly large numbers. In the fixed smear, cells may be seen which are suggestive of clasmatocytes because they have phagocyted parts of other cells or bacteria. In supravital examination these cells cannot be mistaken for any other. Thus, supravital examination of the blood in a case where bacteriæmia may be a factor is a definite diagnostic aid.

Leukopenia is the rule in typhoid, dysentery, "flu," roseola infantum, and measles in the pre-eruptive stage. Pertussis shows a lymphocytosis; pneumonia, appendicitis, abscess formations, etc., show a leukocytosis. Leukopenias may be found in overwhelming infections, or in the unusual reaction of some individuals to the specific infecting organism. This can be illustrated by a white blood count of a case of scarlet fever (Case 1, Table IV). Agranulocytosis is probably a reaction picture of some individuals to certain infections. Oral sepsis is common and is associated with agranulocytosis in a very small percentage. Septicæmias may be associated with agranulocytosis. The blood picture is one of a leukopenia with very few granular cells. It is quite difficult to differentiate from lymphoid leukæmia in the aleukæmic phase.

Infectious mononucleosis and glandular fever give a fairly definite laboratory picture.[18] The leukocyte count varies from 10-16,000 with a differential ranging from 40 to 75 per cent of lymphocytes. The lymphocytes are usually larger on the average than normal. The predominating cell is of the large or intermediate type, having a large amount of cytoplasm surrounding the nucleus. The azure granules frequently are larger and more numerous. The nucleus is often eccentrically placed, and may be oval or kidney shaped.

The laboratory investigation of jaundice cases will indicate the type. The Van den Bergh reaction is direct in the obstructive, and indirect in the hæmolytic. Bile is present in the urine in the obstructive type with decreased stool urobilin. In hæmolytic types of icterus there is no bile in the urine; urobilin is increased in the urine and stools. To thoroughly evaluate any obscure case with jaundice, all these should be estimated.[19]

Arneth counts and Schilling indices of the white cells give a picture of the immaturity of these cells. In any infection there is a shift to the left in the differential count, whether leukocytosis is present or not. The more severe the infection, the greater the proportion of im-

mature cells, and so a greater shift left. The sedimentation test is of no diagnostic importance, but gives an indication of the activity of certain diseases. For instance, in known tuberculosis or rheumatic fever sedimentation tests aid in deciding when the patients may be allowed more activity. Hematocrite determinations on the blood when taken in conjunction with the blood count give the volume of the erythrocytes and the degree of hydration of the blood.

SUMMARY

Many of the variations from the normal hæmatology of infants and children have been illustrated. It is hoped that this discussion will assist the clinician in interpreting laboratory findings.

REFERENCES

1. LUCAS, W. P. AND WASHBURN, A. F., Clinical Pædiatrics, Appleton, N.Y., 1928, **11**: Chap. 3, pp. 23-33.
2. SABIN, F. R., *Bull. Johns Hopkins, Hosp.*, 1923, **34**: 277.
3. ROURKE, M. D. AND PLASS, E. D., *J. Clin. Invest.*, 1920, **7**: 365.
4. BARRON, E. S. G., *Medicine*, 1931, **10**: 77.
5. DAVIS, D., *Am. J. M. Sc.*, 1926, **172**: 849.
6. BLACKFAN, K. D., BATY, J. M. AND DIAMOND, L. K., Oxford Monographs of Medicine, 1930, **9**: Chap. 25, p. 531.
7. BLACKFAN, K. D. AND DIAMOND, L. K., *Am. J. Dis. Child.*, 1929, **37**: 233.
8. DOAN, C. A., *Medicine*, 1931, **10**: 323.
9. LYTTLE, J. D., Clinical Pædiatrics, Appleton, N.Y., 1930, **20**: Chap. 2, p. 26.
10. SNELLING, C. E., *J. Pædiatrics*, 1933, **2**: 546.
11. BATY, J. M., BLACKFAN, K. D. AND DIAMOND, L. K., *Am. J. Dis. Child.*, 1932, **43**: 667.
12. COOLEY, T. B., *Am. J. Dis. Child.*, 1928, **36**: 1257.
13. TILESTON, W., *Medicine*, 1922, **1**: 355.
14. DIAMOND, L. K., BLACKFAN, K. D. AND BATY, J. M., *J. Pædiatrics*, 1932, **1**: 269.
15. MCKHANN, C. F., *Am. J. Dis. Child.*, 1926, **32**: 386.
16. DAMESCHIK, W., *Arch. Int. Med.*, 1930, **46**: 718.
17. ELEY, R. C., *New Eng. J. Med.*, 1932, **206**: 998.
18. ORDWAY, T. AND GORHAM, L. W., *Oxford Monographs*, 1930, **9**: Chap. 19, p. 393.
19. RICH, A. R., *Bull. Johns Hopkins Hosp.*, 1930, **47**: 338.

VECTORS OF RELAPSING FEVER IN RELATION TO AN OUTBREAK OF THE DISEASE IN BRITISH COLUMBIA

BY ERIC HEARLE,

Dominion Entomological Laboratory,

Kamloops, B.C.

A MOST interesting outbreak of relapsing fever occurring in the Kootenay district of British Columbia has recently been recorded by Palmer and Crawford.[16] While this constitutes the first record of the disease in Canada, it has been known for some time in various parts of the United States and has a very wide distribution in other parts of the world, particularly in tropical and sub-tropical regions. The most severe form is found in Africa and India, where the disease is of very common occurrence. In Europe and North America it is usually much milder in form, although serious epidemics have sometimes developed during and following European wars. Various workers have described a number of spirochætes as being responsible for relapsing fevers, but some of the highest authorities, including Wenyon, consider that they are strains of a single species, *Spirochæta* (*Treponema,* etc.) *recurrentis* Lebert. The American form has been discussed by many authors as *Sp. novyi.*

The spirochætes are transmitted by several blood-sucking arthropods, and it is with the insect and tick vectors that we are especially concerned in these notes. In the European epidemics, human lice, and particularly the body louse, *Pediculus humanus corporis* de Geer, are known to be the main transmitting agents and occasional outbreaks in North America have been traced to this source. Bedbugs, *Cimex lectularius* L., have been incriminated, but are generally considered to be of slight importance as vectors. The most important of the transmitting agents are undoubtedly various species of Argasine ticks of the genus *Ornithodorus.* The genus consists of some 13 species and of these at least 7 have been cited as vectors of relapsing fever in widespread areas in Africa, Asia and the Americas. Furthermore, certain species, such as the African hut tick, *Ornithodorus moubata* Murray, have been proved by Dutton and Todd[7] to be infective for life, sometimes as long as three years, and by Möllers (1907) to be capable of passing on the organism through the ova for at least three generations. In general, these ticks resemble bedbugs in their habits, feeding nocturnally, and (in the later stages) for only short periods of less than an hour, instead of becoming attached for days, as

do the members of the family Ixodidæ. In the day time they hide away in cracks and crevices. The larvæ of American forms remain attached to their hosts for several days while becoming replete. Species known to occur in the south-western United States are *Ornithodorus talaje* Guérin-Men., *O. turicata* Duges, *O. coriaceus* Koch and *O. megnini* Duges. The first two have been implicated as vectors of relapsing fever by Bates, Dunn[2] and others. Nothing is known of *coriaceus* as a vector, and *megnini*, the spinose ear tick of cattle, may be dismissed in this respect, because of its very different life history and habits, although Doflein (1911) has indicated that it is capable of such a rôle. All of these species occur in California and *talaje* and *turicata* have been recorded from Texas and the latter also from Arizona (Banks[1]).

Palmer and Crawford (*loc. cit.*) advance the hypothesis that the vector involved in the British Columbia outbreak of relapsing fever is the common "wood tick", *Dermacentor andersoni* Stiles. They state that, "It is our belief that in the cases which are now reported the wood tick has been the vector. It is confidently expected that more cases will appear this year, and we hope that, if such should happen to be the case, it will be possible definitely to prove or disprove this theory."

One of the major projects of the Dominion Entomological Laboratory at Kamloops, B.C., for several years has been a survey of the tick fauna of British Columbia, and much information has been accumulated as to the period of activity of various species of ticks. This information forces the writer to a different conclusion from that arrived at by Palmer and Crawford, since the time of onset of the cases cited is quite at variance with the period of adult activity of *D. andersoni*, and practically eliminates this tick as a possible vector in these particular cases. It should be noted that the incubation period of the disease is short and usually not over a week. In the six case histories given, the illness commenced on June 30, July 27, August 11, August 14, 1932, July 22, 1931 and August 13, 1930.

The season of activity of adult *D. andersoni*, during which attachment to man occurs, is rather well defined in the dry belt of British Columbia and is restricted to the first warm weather of the spring, and on, for a period seldom exceeding two and a half months. It usually commences in the last week of March, reaches a peak in April and recedes in May. The peak of activity in 1932 occurred about April 15 and the season was a normal one. During investigations extending over five years we have only on very rare occasions found adults of this species attached after the end of May. In Montana, according to Cooley,[3] the season may extend to the end of June. The last dates of attachment in our British Columbia records are: 1930, June 29, North Thompson Valley; 1931, July 14, South Okanagan; 1932, June 5, Eagle Valley; 1933, June 24, Nicola. The 1930, '31 and '32 records were from fairly high elevations. It should be stressed that these records are exceptional, being long after the main tick season was over. If *andersoni* was the vector, we should expect the disease to occur during or shortly following the main period of tick activity in April and May, but certainly not in July and August as in the case histories cited.

No other species of tick commonly attacking man are known to be plentiful in the Kootenay district, and Palmer and Crawford state that they have been able "with practical certainty to rule out the louse and bedbug as vectors". It would therefore seem to us to be extremely likely that one of the *Ornithodorus* vectors has become established in the district, rather than that a native species can be involved. There is much to support this possibility. With one recent exception,* only Argasine ticks have so far been incriminated definitely as vectors, and none of the Ixodidæ has been involved. Certain species of *Ornithodorus* are known to have become established far north of their normal range. The spinose ear tick of cattle, *Ornithodorus megnini* Duges, is particularly apt to be transported long distances, since, unlike other species of the genus, it remains attached to the host for very long periods. The main range of *megnini* in North America, according to Hooker, Bishopp and Wood,[11] is Mexico and the lower tier of the south-western United States, and sparsely to Oregon in the north, and from northern California east to Colorado. Like the other species of *Ornithodorus*, it is essentially a southern tick and yet it has become established and has adapted itself to conditions at least as

* Dr. R. R. Parker has brought to our attention Sergent's paper,[19] in which the dog tick, *Rhipicephalus sanguineus*, proved to be the vector in a case of relapsing fever in Algeria.

far north as Alberta. Hadwen[8] records it as having been taken at Lethbridge in October, 1912, and mentions that it was observed by veterinary inspectors some years before that. (See also Hewitt[10]). Professor E. H. Strickland, of the University of Alberta, has sent us specimens taken from jack rabbits at the same locality on December 22, 1931. Dr. R. A. Cooley (*loc. cit.* p. 19) indicates that this tick has been established in Montana for at least sixteen years. Dr. R. R. Parker,[17] of the U. S. Public Health Service tick laboratory, Hamilton, Montana, informs us that he has recently taken *O. turicata* at a mountain camp near Moscow, Idaho, and Dr. R. Matheson[12] has recorded a most interesting occurrence of *O. talaje* in northeastern America. He states,[13] "Though this species is restricted to the tropical and subtropical regions, the author (1931) recorded a typical house infestation in western New York. Here the species has maintained itself for at least four years. Other tropical species may become established, temporarily at least, in our homes and act as agents in transmitting disease."

In the New York case, furniture appears to have been the vehicle for the ticks and doubtless personal effects, such as bed rolls, camping kit, etc., brought in by fishermen and other tourists from the south might be the means of introducing such species as *O. talaje* and *O. turicata* into British Columbia. Migratory birds would seem to us to be another source, and interesting examples of this possibility have been noted. Tick specimens, collected by Mr. A. R. Cummings from a golden-crowned sparrow, *Zonotrichia coronata,* at Vancouver, B.C., on May 2, 1932, and sent to Prof. George Spencer, who forwarded them to the writer for identification, proved to be the fowl tick, *Argas persicus* Oken. The main range of this species in North America (ref. 11, p. 48) is in Mexico and through the southern tier of the United States from California to Florida. The larval stage is the only one in which the tick remains for any length of time on the host, the period of engorgement being from five to six days, but occasionally as long as ten days. This would seem to give ample opportunity for infested migratory birds moving north to transport the ticks long distances. While the fowl tick is mainly known as a serious pest of poultry, it is also sometimes very annoying to man, and has even been cited as a transmitter of relapsing fever (Doflein, 1911), although this has been questioned by Nuttall[14] and his associates. It will be noted that this species and most of the Ornithodori have many habits and characteristics in common.

Perhaps one of the most interesting instances is that of an Ixodid tick, *Ixodes auritulus* Neumann, a species attacking birds, and originally known and described only from the most southerly tip of South America. Hadwen[9] recorded this tick from Queen Charlotte Islands, B.C., where it was taken on June 23, 1910, the hosts being the northern bald eagle, *Haliæetus leucocephalus alascanus* and the Queen Charlotte jay, *Cyanocitta stelleri carlottæ.* The specimens, a male, female and ten larvæ, were identified by Nuttall. (See also ref. 10, p. 227 and Nuttall[15]). This species has come to hand recently on several occasions during our present tick survey, and specimens in the collections at the Kamloops laboratory are from the song sparrow, *Melospiza melodia* (series of twenty-four nymphs taken at Victoria, B.C., July 25, 1932, by J. A. Munro), and from the sooty blue grouse, *Dendragopus obscurus fuliginosus* (one engorged female taken on Pender Island, B.C., by F. Kermode, in September, 1930; another female from S. Pender Island collected by A. R. Spalding on October 30, 1931; and a series of five females taken in the Gulf Islands, B.C., on September 27, 1932, by A. Bryan Williams). Mr. Kenneth Racey, through whose kindness we have secured many interesting tick records, has sent us two nymphs and an adult female from Oregon ruffed grouse, *Bonasa umbellus sabini,* taken at Tofino, V.I., on May 28, 1931. Philip[18] has recently recorded the taking of this species in Oregon on the house sparrow, *Passer domesticus,* this being the first record from the United States. It is evidently now well established in the coast district of British Columbia. Three of the hosts mentioned are resident birds with a very limited range of movement.

Most species of *Ornithodorus* do not appear to have very restrictive host preferences and doubtless also might be transported by migratory birds. Dunn[6] has shown in Panama that *O. talaje* has a remarkable diversity of hosts and will feed on human, mammalian, avian and reptilian blood. He found larvæ of both *O. talaje* and *O. venezuelensis* on chickens, and concluded that probably all domestic fowl may be accepted as hosts. Chicken roosts sometimes

become heavily infested with the former species. The larvæ remain attached for several days before becoming engorged, unlike the nymphs and adults, which feed rapidly after the manner of bedbugs.

Palmer and Crawford's six cases developed in private summer camps at three points along the Lower Arrow Lake. In our experience such cabins, usually utilized for only a short time in the summer for fishing and holiday purposes, almost invariably become the haunts of "pack-rats" (*Neotoma cinerea*). These rats are very plentiful in the less settled districts of the Kootenays, and as soon as a cabin is built they either make themselves at home under the floor or else nest in the proximity and have "the run of the house" by night. They almost invariably winter in vacant cabins, caves or crevices in rocky cliffs and in hollow trees. Their habits render them particularly liable to be important reservoirs of the spirochætes of relapsing fever, and also to act as suitable hosts for *Ornithodorus* ticks during the absence of human tenants. Chipmunks, mice and other rodents might also be factors. Dunn and Clark[5] have brought together considerable information on rats and a number of other mammals as reservoirs of spirochætes and as the possible source of human infections. The common brown rat, *Mus norvegicus*, is considered to be a particularly important disseminating agent in Panama. These authors state that, "Cases of relapsing fever have occurred from time to time in the United States. Several of these apparently acquired their infection while in isolated areas, which would indicate that naturally infected mammals may be concerned in the propagation and dissemination of the disease in the United States". Dunn[4] also, in discussing a house infestation by *O. talaje* in Panama, considered that rats were responsible for bringing in the ticks.

SUMMARY

An outbreak of relapsing fever recorded by Palmer and Crawford as the first occurring in Canada is discussed from the viewpoint of arthropod vectors. The common "wood tick", *Dermacentor andersoni* Stiles, suggested by the authors, is discarded as a possibility in the particular cases cited, since the period of adult activity of this species in British Columbia is from March to May, whereas the cases mainly occurred in late July and August, long after this tick has æstivated. Other native ticks commonly attacking man are unknown in this part of British Columbia, and the suggestion is advanced that one of the well-known Argasine vectors of the spirochæte, such as *Ornithodorus talaje* or *O. turicata*, may have been introduced from the south-western United States or Mexico. Possible means of such introductions and known instances elsewhere are given. *Argas persicus* is recorded from Canada for the first time and new hosts are recorded for *Ixodes auritulus*. Pack rats, *Neotoma cinera*, are discussed as possible factors in the disease, both as reservoirs for the spirochætes and as hosts maintaining the ticks when the summer camps are untenanted.

REFERENCES

1. BANKS, N., Revision of Ixodoidea, or Ticks of the U.S., *U.S.D.A. Bur. Ent. Bull. 15*, 1908, 18 and 19.
2. BATES, L. B., DUNN, L. H. AND ST. JOHN, J. H., Relapsing fever in Panama; the human tick, *Ornithodorus talaje*, demonstrated to be the transmitting agent, *Am. J. Trop. Med.*, 1921, **1**: 183.
3. COOLEY, R. A., The Rocky Mountain Wood Tick, *Montana Agr. Expt. Stn. Bull 268*, 1932, 35.
4. DUNN, L. H., Notes on *O. talaje* infesting a house in the Canal Zone, *Psyche*, 1931, **38**: 170.
5. DUNN, L. H. AND CLARK, H. C., Relapsing fever in Panama with special reference to animal hosts, *Am. J. Trop. Med.*, 1933, **13**: 201.
6. DUNN, L. H., Host selection of *O. talaje* in Panama, *Am. J. Trop. Med.*, 1933,**13**: 483.
7. DUTTON, J. E. AND TODD, J. L., Human tick fever in the Congo Free State, Liverpool School of Trop. Med., Mem. XVIII, 1905.
8. HADWEN, S., in Rept. Vet. Dir. Gen. of Canada for Yr. ending Mar. 31, 1913, p. 80.
9. HADWEN, S., in Rept. of Vet. Dir. Gen. of Canada for Yr. ending Mar. 13, 1915, p. 122.
10. HEWITT, C. G., A Contribution to a Knowledge of Canadian Ticks, *Trans. Roy. Soc. of Canada*, Vol. **9**: Sect. 4, p. 225, 1915.
11. HOOKER, W. A., BISHOPP, F. C. AND WOOD, H. P., Life History and Bionomics of some North American Ticks, *U.S.D.A. Bur. Ent. Bull. 106*, 1912, 63.
12. MATHESON, R., Note on the tick *Ornithodorus talaje*, *Parasitology*, 1931, **23**: 270.
13. MATHESON, R., Medical Entomology, C. C. Thomas, Springfield and Baltimore, 1932, p. 53.
14. NUTTALL, G. H. F., WARBURTON, C., COOPER, W. F. AND ROBINSON, L. E., Ticks—A Monograph of the Ixodoidea, Pt. I, Argasidae, 1908, p. 89.
15. NUTTALL, G. H. F., Notes on Ticks, IV, *Parasitology*, 1916, **8**: 312.
16. PALMER, J. H. AND CRAWFORD, D. J. M., Relapsing fever in North America with report of an outbreak in British Columbia, *Canad. M. Ass. J.*, 1933, **28**: 643.
17. PARKER, R. R., personal communication, Dec. 14, 1933.
18. PHILIP, C. B., The occurrence of *Ixodes auritulus* Neum. in North America (Oregon), *Science*, 1933, **78**: 145.
19. SERGENT, A., Un nouvel agent de transmission naturelle de la recurrente hispano-africaine; la tique du chien (*Rhipicephalus sanguineus*), *Comptes Rendus Acad. Sci. Fr.*, 1933, **197**: 717.

INDICATIONS FOR ABDOMINAL CÆSAREAN SECTION AND THE LOW CERVICAL OPERATION*

BY WM. J. STEVENS, M.D., C.M., F.R.C.S.(C.),

Ottawa

THROUGHOUT the greater part of the last century Cæsarean section was the most fatal of laparotomies. In 1865 the maternal mortality from the operation had reached the appalling figure of 85 per cent. Fifty years ago Max Sänger, an assistant of Credé at Leipzig, first advised the routine use of aseptic uterine sutures and early operation, a contribution which proved the turning point in the evolution of Cæsarean section. Thirty years ago the average mortality was 20 to 30 per cent. In modern times revolutionary changes have occurred in regard to the indications, the technique, and the prognosis of the Cæsarean operation, and, today, conservative figures in the best clinics show the death rate to be between 6 and 10 per cent. In years gone by the operation was used mostly as a last resort after violent unsuccessful attempts at delivery or on women exhausted from hopelessly obstructed labour; today it is preferred to these disastrous efforts at vaginal delivery. Improved technique and knowledge of the conditions requisite for safety have progressively reduced the initial risk, but, regardless of these improvements, the mortality is still excessive. The higher death rate following this particular surgical procedure can be partly explained by the fact that the indications have been gradually extended to include now a number of dangerous pathological conditions, the treatment of which by Cæsarean section has proved the more successful. However, the surgical sacrifice of maternal life has perhaps been contributed to by the occasional indiscriminate performance of the operation when contraindicated, and by faulty methods, while the "desire for action", in the presence of obstetrical complications or dystocia that is only apparent, in preference to delivery by some more legitimate measure, undoubtedly leads to many unfortunate results. It is here that the shop-worn phrase of "masterful inactivity" has its place, for even under the most favourable circumstances the primary risk of Cæsarean section is high, and this makes the decision to perform it always serious. The operation is nearly seven times more dangerous than natural delivery. The justification for its performance is, therefore, of paramount importance.

* Read by invitation before the meeting of the Ontario Medical Association, Hamilton, June 8, 1933.

THE INDICATIONS FOR ABDOMINAL CÆSAREAN SECTION

These are:

1. Cephalo-pelvic disproportion.
2. The hæmorrhages of late pregnancy.
3. The toxæmias of late pregnancy.
4. Cases complicated by systemic diseases, etc.
5. A previous Cæsarean section.

Cephalo-pelvic disproportion. — Contracted pelvis is the most frequent indication for Cæsarean section, accounting for about 60 per cent of the cases. Disproportion, whether due to absolute or borderline contraction of the pelvic canal, or to the baby's head being too large for the mother's pelvis, may be dealt with in several ways.

First, "elective Cæsarean section." The prime objective of scientific obstetricians is to predetermine in all cases that method of delivery which will give the best result for both mother and child. In dystocia, the obstetrician should be able to determine before labour, especially at term, the nature of the labour and the indications for its management; whether a woman will be delivered spontaneously or by low forceps; or whether abdominal hysterotomy (elective Cæsarean section) will be necessary. Careful, early, antenatal pelvic measurement, confirmed during the last month, should discover definite or borderline evidences of pelvic deformity and act as a preliminary point in deciding the best method of delivery. We must also consider the father, his comparative physique, and especially the size of his head, together with the obstetric history of the patient's mother. Measurements and the fitting of the fetal head to the pelvis in the last two weeks of pregnancy, digital

examination, and x-rays, all serve to give a definite conception of disproportion and of the possibility of spontaneous delivery. In applying the Müller test under anæsthesia, failure of the head to enter the inlet constitutes "elective Cæsarean section" as the best and safest method of delivery, preferably before onset of labour, with the membranes intact, and in the absence of vaginal examinations or manipulations, which desirable conditions are all important in tending to lower the mortality and morbidity rates. In practically all cases where the sacral promontory is readily reached the stamp of contracted pelvis may be put on. It is our general rule to operate upon patients who have an internal conjugate of less than 8 c.m., an external conjugate below 17.5 c.m., or a transverse less than 8 c.m. accordingly. In the male type of pelvis, the heavy-set masculine woman with short extremities and narrow rigid outlet, with perhaps a previous long disastrous delivery, as in the elderly primipara, with even slight pelvic contraction, and with one healthy baby as a vital consideration, the protracted labour often makes abdominal delivery safer.

Secondly, early "induction of labour", particularly in the young primipara, must be given consideration at the 8th month or so, where the head could be made to enter the pelvic inlet, depending upon the degree of disproportion.

Thirdly, a "test of labour" may be given, particularly in the borderline case. Sometimes we may over-estimate the importance of pelvo-fetal disproportion, especially if we do not give the head a thorough opportunity to mould. The floating or high head, apart from disproportion, malposition or malpresentation, is frequently caused by uterine motor dysfunction or temporary incoordination, an absence of upper segment sustained contraction and retraction, indicated clinically by an arrest or a prolongation of cervical effacement and dilatation which renders descent of the fetus ineffective. In those doubtful cases, managed expectantly, afforded rest by analgæsia, and given sufficient liquid food, after one hour or more of powerful unproductive five-minute pains, with full dilatation and ruptured membranes, the fetal heart and maternal weakening may indicate whether the labour should be terminated abdominally or vaginally. Otherwise the "test of labour" may constitute 6 to 12 hours or longer of strong, active uterine contractions, which, resulting in floating head, no attempt at engagement, ineffective progress, and a weakening fetal heart; accordingly resort is made to Cæsarean section, the criteria for which are dependent upon the experience and judgment of the obstetrician and the individualization of each case. However, failure of the test, ending in vaginal delivery, by strenuous forceps, version or craniotomy, may result in such perineal mutilation, muscle detachment and bony separation, with a damaged or dead baby, as to actually make the prognosis worse than in the case of a properly-timed Cæsarean section.

The hæmorrhages of late pregnancy.—In "central placenta prævia" one must consider each case individually, but, regardless of the parity or period of gestation, abdominal Cæsarean section must be considered, and here the high classical operation may be preferable. In all primiparæ and in most multiparæ having a closed or slightly dilated cervix, at or near full term, with a living baby and the mother in good condition Cæsarean section is best, while small pelvic measurements, or a large child associated with "complete or partial placenta prævia", only make the indications more pronounced. In recent years there has been a tendency to resort to section in these cases more often than previously, and the results show a reduction in the mortality rates, particularly for the baby. Section is indicated wherever any difficulty or delay would be necessary to accomplish vaginal delivery. Vaginal examination should be avoided.

"Marginal, lateral or low-attached placentæ" should be treated accordingly, taking into consideration the parity, the amount of dilatation, the viability of the child, and the general condition of the patient. With a well-dilated or dilatable cervix, a proper sized child, and a placenta not occluding the os, early vaginal delivery may be successfully accomplished.

In "accidental hæmorrhage" Cæsarean section is often favoured, unless the patient will deliver or can easily be induced and delivered without delay, together with blood transfusion. Especially, in the acute, complete placental separation, a classical Cæsarean section, with or without hysterectomy, is often best.

Pre-operative "blood typing and transfusion" must never be neglected, or as a temporary

measure, glucose-saline intravenously, before, during, or after delivery, especially in all hæmorrhage cases. In seriously exsanguinated patients every effort is made to save blood, and shock is first treated with morphine and blood transfusion. Where post-operative uterine bleeding persists excessively after placental removal, or prophylactically as a routine, consideration can be given to packing the uterus with a wide strip of 10 per cent iodoform gauze, pushing the end down through the cervix, which thus acts as a tampon and assists drainage or otherwise, packing the uterus from below, plus immediate transfusion. Pituitrin intravenously and ernutin hypodermically are given and measures taken to prevent shock.

Serious "post-Cæsarean hæmorrhage", the result of uterine atony, where the placental attachment was over a previous thin, imperfectly healed Cæsarean scar, the fibrous tissue of which impairs the control of hæmorrhage, may be avoided by complete excision of the scar. Otherwise, as in the critical toxæmia case, where intramuscular hæmorrhages inhibit uterine contractions, the failure of intensive conservative measures—transfusion and packing—sometimes renders hysterectomy with transfusion imperative before it is too late.

The toxæmias of late pregnancy.—In the "severe pre-eclamptic" patient or the "fulminating nephritic" at or near term, who under intensive well-directed medical treatment shows no improvement in the toxæmic condition, with no engagement and an elongated thick cervix, Cæsarean section has its place after attempts at more conservative induction have been made. Sometimes a moribund patient is sectioned in the interest of the child.

In "eclampsia" Cæsarean section should be definitely discouraged, as the mortality rate is unjustifiably high, averaging over 25 per cent in the very best clinics. The operation, as a rule, does not cure or relieve the convulsive seizures, except by death, which is poor compensation for the cessation of vigorous eliminative treatment, etc. There is a definite well-warranted tendency to conservatism in the toxæmias where convulsions are occurring, and the lower death rate of late years can be attributed in part to the comparative infrequency of Cæsarean sections in eclampsia. Only where the convulsions have ceased for 12 hours or so in a highly resistent eclamptic, with an unengaged presenting part, a rigid cervix and a living baby, with failure to respond to 24 hours or more of active sedative eliminative measures and to all other attempts at induction, Cæsarean section may be considered. In the presence of active cephalo-pelvic dystocia or other urgent obstetric indications, such as premature placental separation during the eclamptic attack, section may be done, regardless of the poor operative risk.

Cases complicated by systemic diseases, etc.—Serious heart disease, advanced tuberculosis, diabetes, exopthalmic goitre, epilepsy and other constitutional disturbances—very poor risks for labour or the production of a living child—are being treated, accordingly, more often by abdominal delivery. Especially, the rheumatic mitral stenotic, over 35 years of age, with acute or congestive failure, cardiac patients conceded to be bad prospects for prolonged labour, or with obstetric indications, are best treated by Cæsarean section and sterilization at the proper time. Strict individual medical-obstetric care from early in pregnancy or before, with complete rest in bed at the onset of any indisposition or overexertion, is absolutely essential, and hospitalization for 6 weeks or until delivery if decompensation threatens. The classic operation saves time; the patient's energy is thereby more conserved from shock and trauma than in the case of either a spontaneous or an instrumental labour. The cooperation of a cardiologist and an anæsthetist is desirable. In diabetics, competent insulin control with Cæsarean section about 3 weeks before term is more apt to secure a living child. "Sterilization", should be considered or urged, especially at the time of the second section, if the previous child is alive, for these debilitating cases or for other mental or physical infirmities.

"Pathological pelvic indications" cover cases which as the result of previous gynæcological operations now necessitate Cæsarean section in labour, such as amputation or repair of the cervix, uterine suspension, extensive plastic operations, and adhesions. Other conditions, such as fibromyomata uteri, ovarian tumours, bicornuate uterus, rupture or hernia of the uterus, contraction ring, osteoma, congenital obstructive malformations, varicosities of the vulva and vagina, acute polyhydramnios, hydrops neonatorum, or previous inexplicable stillbirths, often require Cæsarean section, some, Cæsarean-

hysterectomy, especially in the presence of definite sepsis. Cervical stenosis, after a reasonable test of labour, or uterine inertia, with the sudden appearance of fetid liquor amnii in primiparæ or multiparæ, may call for Cæsarean section before the death of the fetus. In early operable carcinoma of the cervix, vagina or vulva, proved by biopsy, operate at once; if inoperable, do a Cæsarean section, followed, perhaps, by wide panhysterectomy near the end of pregnancy.

"Transverse presentation", with a live baby and early ruptured membranes, especially if associated with pelvic complications, as is frequently the case, often indicates early Cæsarean section. A "neglected shoulder presentation", with threatened uterine rupture, may also require it. "Breech presentation" with long rigid cervix and prolapse of the cord or extended legs, especially in the borderline or old primipara, with a live baby showing fetal distress and no progress, often demands it. Craniotomy is the method of choice where the child has died *in utero,* in extreme sepsis, or in hopelessly impacted presentations.

X-rays should indicate anomalies — hydrocephalus or twins.

A previous Cæsarean section. — "Once a Cæsarean, always a Cæsarean?" The majority seems to favour it, as being safer. The danger of uterine rupture is usually given at 4 per cent after the classical incision. The sooner a second pregnancy occurs after a Cæsarean section, the greater the necessity for another abdominal delivery. The question of re-section in subsequent pregnancies, sometimes depends upon whether the patient showed a temperature indicating any morbidity when convalescing from the previous operation, suggesting uterine wound infection with poor uterine scar formation. A faulty method of uterine wound closure is to be considered. Further, if the placenta happens to develop immediately upon the inner surface of the old wound, the tendency of the syncytial cells to invade the uterine wall so weakens the uterine scar by absorption that rupture may take place. A previous Cæsarean section for dystocia generally indicates further section.

However, "once a Cæsarean," should not necessarily mean, "always a Cæsarean." If a Cæsarean section has been done previously for premature separation, central placenta prævia or toxæmia, or if the baby is small or non-viable, a test of labour may be given in hospital during the next labour if the patient is normal. The patient may be carefully observed prenatally, dieted, x-rayed and induced at 8 months or so, and preparations made to deal promptly with any threatened rupture during labour, by hysterectomy or suture, according to the exigencies of the case.

THE OPERATION

The "low cervical" or intraperitoneal retrovesical Cæsarean section is gradually receiving better recognition, giving as it does, a much lower mortality rate than the popular classical operation, while the extraperitoneal Cæsarean, the Porro operation, and other modifications, are performed as a rule only in very bad operative risks.

Two days prior to operation, where the elective Cæsarean section is contemplated, the patient is given a cathartic and advised to restrict her diet to light articles, with abundant fluids. At least 24 hours prior to operation the patient is admitted to hospital, when the usual laboratory tests and careful physical examination are done. On the day preceding operation the laparotomy and vaginal preparation is done with shaving, washing the abdomen and external genitals with gauze, tincture of green soap and warm water, then with ether, then alcohol, using sterile gauze, after which the abdomen is covered with sterile towels and the vulva with a sterile pad, which is fastened to a T-binder. The patient is given a soap-suds enema and a 3-quart vaginal douche with 1:5000 potassium permanganate at 110 degrees F. if deemed expedient. On the day of operation she is given fluids only by mouth. Six hours prior to operation she is given a second soap-suds enema, and 3 hours before, a second potassium permanganate douche if necessary. One hour prior the patient is catheterized and given 1/150 gr. of atropine sulphate hypodermically. On the operating table the abdomen is thoroughly painted with 5 per cent tincture of iodine and then draped.

Operative technique.—The patient is anæsthetized with a minimum of gas-oxygen-ether, and placed in a modified Trendelenburg position, or local or spinal anæsthesia may be used. A longitudinal median abdominal incision, about 5 to 6 inches long, is made from below the umbilicus to the symphysis pubis. The skin, subcutaneous tissue, and fascia are incised, the rectus muscles separated, the peritoneum exposed, in-

cised and opened with scissors, care being taken to avoid injuring the bladder which is retracted. The upper and lateral portions of the abdominal cavity are protected with laporatomy towels, and a lateral retractor is put in place under the peritoneum on each side. A shallow, transverse semilunar incision, about 15 c.m. in length, with the convexity downwards, is made through the uterine serosa, about midway between the grey line of the contraction ring and the bladder reflection. With gauze on the finger the two peritoneal flaps are separated, raised, and the ends held by sutures with forceps. One-half c.c. of pituitrin or of pitocin, diluted in 3 c.c. of normal saline, is now given intravenously. The bladder retractor is placed over the lower flap to hold it down, thus exposing the denuded lower uterine segment, which is similarly incised transversely, for about 15 c.m., also with the convexity downwards. This is opened with a scalpel in the centre and the incision is completed with bandage scissors on each side. The suction apparatus is introduced and continuous aspiration of the fluid and blood is maintained. The upper and lower edges of the uterine incision may be held with Allis forceps or tongue clamps. If the anæsthetist now gives a whiff of oxygen to the mother it tends to produce a lusty crying baby. The baby's head is gently shelled out on the palm of the hand or in the concavity of a single forceps blade, assisted by pressure on the fundus. The placenta and membranes are withdrawn completely, through the incision.

The uterine incision is very carefully closed with continuous No. 2 chromic catgut sutures, the first suture including wide bites of the lower muscular layer, and the second the upper muscular layer and fascia of the now well contracted lower segment. The uterine peritoneum is now closed by anchoring the edge of the upper flap under the lower flap with 7 or 8 interrupted sutures, in such a way as to permit the lower flap to be raised and overlap this line of interrupted sutures. The second line of the double-flap closure is completed above with a continuous No. 2 chromic catgut, thus doubly sealing off the uterine incision and preventing leakage of infected material from the uterus into the peritoneal cavity. The abdominal pads are now removed, and the abdomen is closed in three layers, skin clips are applied, the wound is iodined, and a dry dressing put on, which is completely covered with snug adhesive straps, and a Scultetus binder is applied, plus a sterile vulvar pad. Careful post-operative care is instituted.

THE ADVANTAGES OF THE LOW CERVICAL OPERATION

1. The mortality rate of low cervical Cæsarean section is less than one-half that of the old, or classical procedure.

2. In infected, prolonged labours, this operation is specially suitable, as the lower uterine segment resists infection better than the fundus.

3. The danger of general peritonitis is very much lessened; the spill is more accessible and any infection is restricted to the lowest part of the abdomen, favourable to localization and evacuation.

4. Post-operative discomforts are less and adhesions fewer, as the intestines and omentum are seldom seen or handled during the operation.

5. Sutures in the passive lower segment are afforded more protection and less strain from muscular activity, providing for a stronger scar, with a lessened liability to uterine rupture in any subsequent labour.

6. The adequately long, transverse semilunar incision of 15 c.m. or more is restricted to the thinner, avascular, lower uterine segment, where the muscles and blood vessels run transversely, thus permitting, with reasonable care in delivering the head, of very little trauma and much less hæmorrhage than with the classical operation.

Otherwise, this operative technique is somewhat more complicated and takes a little longer to perform than the classical.

CONCLUSION

While the successful Cæsarean operation is unique, in that two lives are saved instead of one, it must always be regarded with the utmost respect and never subjected to the danger of incurring that familiarity which breeds contempt. The operation is extremely hazardous and should be undertaken only after the most careful consideration of every factor involved. We must continue to seek the means of placing it on a firmer basis. The mortality rate in Cæsarean section depends on the judgment and ability of the operator, with due regard to the indications for its performance, the condition of the patient, the time of operation, and the type of operation. The mortality rate in the low cervical operation is so much lower than in the classical, that a more universal adoption of this operation, with curved transverse incision and double-flap closure, for most cases should seem reasonable.

THE PREVENTION OF MATERNAL INJURY INCIDENT TO PREGNANCY, FROM THE STANDPOINT OF THE GENERAL PRACTITIONER.—In the prevention of maternal injury incident to pregnancy and labour, P. Brooke Bland discusses some of the common conditions that may lead to serious injury. They are: in the first trimester, pregnancy not within the uterine cavity, but within the Fallopian tube, the premature expulsion of an indwelling uterine pregnancy, and abortion; in the second trimester, hydramnion and hydatidiform mole; in the third trimester, toxæmia and rupture of the uterus; injuries incident to labour; mechanical factors; prevention of injuries incident to tubal gestation; injuries incident to abortion; hydatidiform mole; injuries from pregnancy toxæmia; rupture of the uterus; injuries of the cervix; injuries of the perineum, and damage from sepsis.—*J. Am. M. Ass.*, 1932, **99**: 1937.

A CASE OF HODGKIN'S DISEASE WITH MARKED EOSINOPHILIA

BY D. F. COBURN, M.D. AND J. E. PRITCHARD, M.D.,

Montreal

THE abnormal blood findings in this case of Hodgkin's disease are so unusual as to be worthy of record.

The patient, a French-Canadian woman of 49, entered the Montreal General Hospital on January 29, 1931, being admitted to the service of Dr. Campbell P. Howard. Her complaints were as follows: swelling of the abdomen and right lower limb, with shortness of breath and weakness for the past two years; constipation and yellowness of the skin for many years, but she was vague as to the latter symptom; palpitations; paralysis of the right extremities and the right side of the trunk; loss of weight and a burning sensation while voiding, all for the previous six weeks.

Personal history.—The patient was born in Canada, and had had a healthy childhood. She bore 13 full-term children, 9 of whom are alive. She had an operation for a non-toxic adenoma of the thyroid in 1927, and a years later the present illness began. She had never been troubled with headaches, earaches, impaired hearing, or discharge from the ears. She had had a moderate number of head colds, usually in conjunction with indigestion. There was no history of a sore tongue or of sore throat. Decay caused her to have most of her teeth removed. In 1912 she noticed a swelling in her neck, which gradually increased. Before her operation in 1927 she complained of nervousness, irritability, palpitation, loss of strength, loss of six pounds of weight in six months, dyspnœa, cough and constipation. She had had no respiratory symptoms except that during the past one or two months she had a morning cough. She had had no œdema of the feet and ankles, and no pain about or radiating from the heart. Her appetite was usually quite good. Three to four years ago she had digestive upsets, with severe pain in the upper abdomen and burning beneath the lower part of the sternum on several occasions. At the same time she had pain in the region of the lower thoracic vertebræ. She had had only occasional vomiting, with no hæmatemesis, no hæmorrhoids, no bright blood in the stools, no tarry stools, and her stools had been light in colour for an indefinite period. She had had no nocturia, frequency, pain or burning with micturition.

Her menstrual history was normal. She had lost a little weight.

Family history.—Negative.

Present illness.—Her present illness began about two years ago, when she noticed some swelling of the lower abdomen and the right lower limb. This swelling and, in addition, weakness in the right upper extremity, had gradually become more marked. The patient began to have fullness in the epigastrium, with discomfort and considerable gas after food—fluids especially—two years ago. These upsets were only occasional, were associated with chills and fever, and were followed by yellowness of the skin, loss of strength and fatigue. She thought that her skin had been somewhat yellow since her first pregnancy, thirty years before. She had had some dyspnœa for the past two years, but this and the above-mentioned symptoms had not been incapacitating. On December 9, 1930, she noticed that her right arm was considerably weaker, and that the following three days she became generally weaker. On December 12, the right side of the body, the face excluded, was paralyzed, and shortly after being put to bed she became unconscious. She was able to swallow, but had incontinence of urine, though not of fæces. After three days she was able to speak a little, and could move the right side of the body slightly. She had been unable to walk since December 12, 1930, and had remained in bed. During this period she had had some burning with urination, and mild palpitation.

Physical examination.—The patient appeared sick, and her colour was sallow, almost icteroid. The tongue showed early atrophy at the edges. There was pitting œdema of the right side of the trunk and the right lower extremity. Over the anterior and posterior surfaces of the left forearm were scattered petechial hæmorrhages. On the dorsum of the lower half of the right forearm was a triangular area about three inches long, composed of numerous small ecchymotic areas, present for two days. The right limbs were moved but little.

There were some badly decayed teeth. The sensorium was clear and the cranial nerves intact. There was some increase of reflexes of right arm and leg, with a suggestive extensor response to Babinski stimulation on the right.

The lungs showed some basal moisture. The heart action was slow and regular, and a very soft systolic murmur was audible everywhere. Blood pressure (left) 90/50. The aortic second sound was slightly tapping.

The abdomen was much enlarged, with the umbilicus pouting. The veins were just visible in the upper half No organs were palpable, but satisfactory palpation was impossible . There was a definite fluid wave.

The pelvic outlet was relaxed, multiparous, and there was a moderate cystocele. Along the left pelvic wall a mass was felt, the size of a hen's egg, not tender, with only one surface palpable. There were no hæmorrhoids and the sphincteric tone was good. About three inches above the anus a mass was detected, shaped like a blunt cone, smooth in contour, not tender, and firmly fixed anteriorly.

There was generalized enlargement of the lymph nodes. The epitrochlears were small but palpable; the anterior and posterior cervical lymph nodes were small and firm; the occipital nodes not felt. Palpable axillary nodes were noted bilaterally, somewhat enlarged, discrete and almost stony hard. There were several large inguinal nodes, more marked on the right side. There were a few small, palpable popliteal nodes. Over the sixth rib in the left mid-axillary line was a small, firm nodule, movable under the skin and over the rib.

Diary.—January 31, 1931. Abdominal paracentesis was done. The peritoneum did not seem thickened, but it was tough. Four hundred cubic centimetres of straw-coloured fluid were removed. The condition of the patient was good. The liver and spleen were not palpable.

February 6, 1931. The general appearance of the patient was better. Under the left costal margin there was thought to be a palpable mass, suggesting the spleen, and in the right upper quadrant a more superficial mass was palpable, with a sharp edge, descending on inspiration. An abdominal paracentesis was done and 900 c.c. of dark yellow fluid were withdrawn. The liver edge was felt two finger-breadths below the right costal margin. In the left upper quadrant a mass was palpable (only part of the time). Deep palpation a few centimetres above the umbilicus enabled one to feel nodules within the abdomen, not fixed posteriorly. Rectal examination again revealed a mass palpable along the right anterior

wall of the rectum, three inches above the anus. This mass was the size of a hen's egg, was rounded and very firm except at its tip, which was less firm but not soft, was tender, not movable, and was attached to the bony pelvis along the right.

February 14, 1931. Under local anæsthesia a biopsy of the left axillary lymph nodes and the left biceps muscle was performed.

February 15, 1931. About 9.45 a.m., the patient complained of difficulty in breathing. Râles were heard throughout the chest. She improved for two hours after receiving morphine, atropine and intravenous glucose (25 per cent). Her condition in the early afternoon became worse and stimulants failed to aid her. She died at 5.10 p.m.

Report of the hæmatology laboratory (1-29-31.).—Red cells, 4,020,000; hæmoglobin, 83 per cent; reticulocytes, 1.4 per cent; red cell diameter, 7.4 microns; platelets, 170,000. Differential count: neutrophilic polymorphonuclears, 9; lymphocytes, 8; myelocytes, 2; basophiles, 2; eosinophiles, 79 per cent; Type 1, 29; Type 2, 39; Type 3, 11; Type 4, 0. The red blood cells show some basophilic stippling. No nucleated forms seen.

Urine.—Sp. gr. 1014-1022; acid; albumin 0-trace; glucose, 0; occasional leucocytes, once; occasional hyaline casts.

Fractional meal.—Free HCl and total acidity normal. Occult blood was found in four of the five specimens examined. No demonstrable bile. Microscopic examination, epithelial cells.

Stool.—Six specimens examined. No ova or intestinal parasites seen. Occult blood found in four of the specimens.

Spinal fluid.—Clear. Pressure, 110 mm. H_2O; globulin, 0; cells, 20, all lymphocytes. The Wassermann test and colloidal gold curve, negative.

Blood Wassermann.—Negative.

Metabolism (1-30-31).—Blood sugar, 0.084 per cent; urea nitrogen, 14.0 mg. to 100 c.c.; creatinine, 1.22 mg. to 100 c.c.; van den Bergh, indirect, 0.2 units; urobilinogen present in 1 to 100 dilution. (1-31-31). Uric acid, 2.50 mg. to 100 c.c. (2-2-31). Basal metabolic rate, –14. (2-9-31). Urobilinogen present in 1 to 100 dilution.

Electrocardiographic report.—Delayed A-V conduction (0.21 sec.). T inconspicuous. Low E.M.F. Regular rhythm.

X-ray (1-30-31).—*Chest.* A small collection of fluid or pleural thickening in the right costo-phrenic angle. The irregular mottling through the right lung suggested resolving pneumonia. There was some increase in the transverse diameter of the heart. *Abdomen.* Marked dilatation of the stomach by gas. (2-4-31) *Chest.* Heart slightly enlarged. Scattered areas of consolidation through the right lung resembling broncho-pneumonia. (2-7-31). Long bones, negative. (2-9-31). Barium series; a suggestive barium rest present in the first part of the duodenum at twenty-four hours. (2-12-31). Barium enema, negative. Abdomen; opaque shadow at the level of the right transverse process of the second lumbar vertebra. Two more opaque shadows at the level of the right transverse process of the fifth lumbar vertebra.

CONSULTANTS' REPORTS

Neurologist.—"The patient has had a right-sided hemiparesis, and there is now paresis of the right arm with slightly increased reflexes of the right arm and leg, while there is an extensor response to Chaddock stimulation and suggestive extensor response to Babinski stimulation on the right side. No sensory disturbance made out. The lesion is probably thrombotic in origin; etiology unknown."

Gynæcologist.—"The pelvis is negative."

Surgeon.—"The enlargement of the lower right limb is due to blockage of the lymphatics by enlarged inguinal nodes. Suggest biopsy of axillary nodes."

Biopsy report.—"Sections of the lymph nodes show complete replacement of the normal architecture by a diffuse cellular structure. These cells are composed of lymphocytes, numerous large endothelium-type of cells, and an enormous number of eosinophiles. No definite lymph follicles are seen. Throughout the nodes there appears to be swelling of the vascular endothelium, but no increase in connective tissue. Occasional mononuclear giant cells are seen. Sections of the muscle show here and there foci of lymphocytes and eosinophiles, but no parasites have been located. There are also small hæmorrhages, and the muscle bundles have been separated by œdema. Diagnosis—acute Hodgkin's disease."

LABORATORY FINDINGS

Blood	1-29-31	1-30-31	2-3-31	2-11-31	2-15-31
Red blood cells	3,300,000			3,105,000	
Hgb. (Sahli)	72 per cent			73 per cent	
Platelets					284,000
White blood cells	30,250		31,050	38,000	
Differential count					
Neutrophilic polymorphonuclears	2	3	10	4	18
Lymphocytes	3	3	3	4	8
Mononuclears	0	0	0	0	4
Basophiles	0	0	1	0	1
Eosinophiles	94	93	86	92	69
Polymorphonuclears	58	55	67	67	45
Metamyelocytes	30	32	17	24	24
Myelocytes	6	6	2	1	0
Neutrophilic myelocytes	1	1	0	0	0

The red blood cells appeared to be of normal size, shape and colour.

AUTOPSY FINDINGS (CONDENSED)

The pleural cavities each contained 1,000 c.c. of clear, dark-brown fluid. One or two soft adhesions were also found in the left pleural cavity. No mediastinal mass of glands was found. The usual number of peribronchial nodes, of a dark, greenish-black colour, were encountered. The pericardial cavity contained 400 c.c. of clear, straw-coloured fluid. The heart and lungs showed nothing of note. The "sentinel" node was large and firm.

The peritoneal cavity contained 1,000 c.c. of clear, straw-coloured fluid, and the peritoneum was everywhere smooth and glistening. The liver reached two finger-breadths below the costal margin, was rather firm, and of a pale, reddish-blue colour. The lower portion of the abdominal aorta was surrounded by a firm mass of nodes and scar tissue, partially compressing it. This mass extended downwards to the bifurcation, whence a mass extended down each lateral wall of the pelvis, that on

the left being the larger. A mass of nodes also lay about the right iliac vessels along the brim of the pelvis, constricting the lumen of each. There were firm hard nodes about the head of the pancreas in the gastro-hepatic omentum, and less firm, but enlarged, nodes in the mesentery of the small intestine.

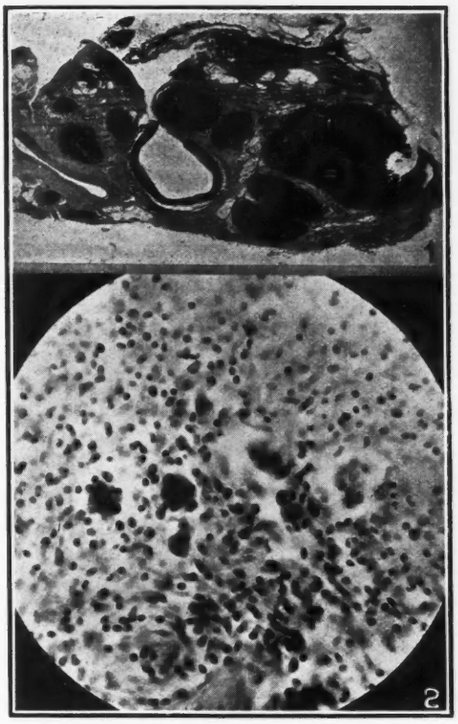


FIG. 1.—Section through the retro-peritoneal tissues, showing aorta, vena cava, involved nodes and extensive fibrosis.

FIG. 2.—Photo-micrograph (high power) of lymph node. Note multinucleated cells (Sternberg giant cells).

The spleen weighed 300 grm. and was soft. The liver showed passive congestion. The other viscera showed nothing remarkable. The stomach and intestines presented no lesions, but there were innumerable, small, grey, opaque areas, 1 mm. in diameter, in the mucosa of the proximal half of the colon. The bone marrow of the vertebræ was dark red in colour and not specially soft, while that of the femur was pinkish-grey in colour. Lymph nodes from various regions were all enlarged, quite firm (some very hard), and of a shiny homogeneous appearance on section, though a few showed minute hæmorrhages. About each mass of nodes was dense, white, shiny, tough scar tissue, and in it the nodes remained discrete.

The brain weighed 1,380 grm. and showed no gross lesion, other than injection of many small vessels.

Microscopic examination.—The lungs showed engorgement of the vessels, with many red cells in the alveoli. In the vessels of the alveolar walls were many eosinophiles, the greater number of them being polymorphonuclear. Considerable œdema of the bronchial walls was noted throughout. The most noticeable feature was the diffuse infiltration of the connective tissue by an exudate consisting of large mononuclears, eosinophiles, a few multinucleated giant cells, a few plasma cells, and an occasional polymorphonuclear neutrophile. The right ventricle of the heart showed an increase of connective tissue throughout. The outer half of the wall of the left ventricle was normal, while the inner half exhibited patches of degenerated muscle, and complete absence of some muscle bundles with replacement by connective tissue. In this inner layer of the ventricular wall were many eosinophiles, phagocytic cells, mononuclears and lymphocytes.

The normal architecture of the spleen was preserved; the follicles were distinct, and composed of lymphocytes, with here and there scattered eosinophiles. The red pulp, including both the sinusoids and Billroth cords, was engorged with eosinophiles. There was a great hyperplasia of the pulp, chiefly of large, polyhedral mononuclear cells with vesicular cytoplasm and prominent nucleoli. Scattered throughout were numerous mono- and multi-nucleated giant cells, with hyperchromatic nuclei and multiple nucleoli. The sinus endothelium was hyperplastic. In some of the splenic veins of the trabeculæ was an intense infiltration of the vein wall with cells consisting almost entirely of eosinophiles. These had practically obliterated the architecture of the veins; the lining epithelium could be identified, but this and the connective tissue of the trabeculæ was in the broad zone of closely packed eosinophiles with occasional lymphocytes. Even the connective tissue of the trabeculæ was infiltrated with the same type of cell.

The sections of the liver showed marked congestion, with the central areas of the lobules filled with blood, which was compressing the liver cords. Numerous eosinophiles were present in the blood in the sinuses, and the portal spaces showed the same type of infiltration which prevailed throughout the lungs.

The capsule of the pancreas showed quite marked infiltration, chiefly with eosinophiles; several large nodes in these sections showed the changes described under nodes elsewhere.

The adrenals and pelvic organs manifested no changes.

The aorta contained some small atheromatous plaques, but no calcification was seen.

No lesion was seen in the sections of striated muscle.

Sections of the bone marrow presented a compact cellular structure with very little fat, consisting almost entirely of eosinophilic cells, the majority of which were mononuclears; numerous lymphocytes were also present, as well as large megakaryocytes and eosinophilic myelocytes.

The lymph nodes everywhere showed replacement of their normal structure by diffuse cellular material in which one saw: (1) a diffuse reticulo-endothelial cell hyperplasia, with a variable number of, but few, Sternberg giant cells; (2) a diffuse eosinophilic infiltration; (3) a variable amount of fibrosis, from very little to very marked scarring; (4) a great increase in the reticular structure, as seen with Laidlaw's stain. In some nodes were small dense collections of eosinophiles which were partially necrotic, suggesting small abscesses. In the retroperitoneal tissue, the nodes were embedded in great masses of scar tissue, and it was in these especially that fibrosis and atrophy had occurred. The retroperitoneal tissue itself consisted of dense broad bands of connective tissue containing vessels and nerves, with intervening fatty tissue. There was considerable patchy infiltration with lymphocytes and eosinophiles.

Brain (Report from the Department of Neuropathology, Royal Victoria Hospital, Montreal).—The meningeal and cerebral vessels were engorged with erythrocytes and eosinophiles, standing out brilliantly. Many of the smaller vessels showed proliferation of the endothelium of their lumina, but no total occlusion. In the right occipital lobe, bordering between the grey and white matter, was an area where the nervous elements had entirely disappeared and had been replaced by granular, fat-filled phagocytic cells, with a few red cells. No attempt at repair in this area was seen, and there was no evidence of an inflammatory process. The same picture was seen, to a lesser extent, scattered through the brain substance. An occasional brilliantly-stained eosinophile was seen within the brain substance, and a

few small hæmorrhages had occurred, but seemed to be confined to the perivascular spaces. There was considerable increase of glial tissue, often in foci. Satellitosis was present in a few areas. Some of the ganglion cells appeared to have suffered, their nuclei being in an eccentric position. In the region of the fissure of Sylvius an aneurysmal dilatation was present in the wall of a large vessel, the tunica media being entirely deficient. No rupture had occurred. No other changes in the larger arteries seen. Arachnoid whorls were numerous and there were many psammoma bodies. The ependyma was thickened in many regions and denuded in others.

The changes consist, then, of moderate arteriolar and capillary thickening, with small foci of softening. While there was no gross difference in this process on the right and left sides, minute sectioning at various levels might have explained the right-sided weakness. The fluctuation of motor signs is understandable on the basis of small focal softening with œdema surrounding these areas, followed by resolution and disappearance of the œdema with improvement of the clinical picture. The factor in the production of the focal softening must be the vessel narrowing. No Hodgkin's nodules were found in the brain and the changes were not those usually associated with the leukæmias. Diagnosis—cerebral softening, focal, due to vascular lesion.

The interest aroused by this case led to a search of the literature for similar cases of Hodgkin's disease with an eosinophilia. Lincoln[1] reports a case, confirmed at autopsy, in a boy of fifteen, the white blood cells numbering 49,000, and there being as high as 68.2 per cent of eosinophiles present. Sanguinetti[2] mentions a patient (a young woman) with 30,000 leucocytes with 85 per cent of eosinophiles. Biopsy of a cervical node revealed the presence of Hodgkin's disease. A case of Hodgkin's disease coming to post-mortem, with from 20 to 50 per cent eosinophiles in a white cell count of 8,000 to 11,000, is reported by Weber.[3] Allen and Thro[4] present the findings of a male, aged 32, with slightly enlarged nodes and an enlarged spleen, who had from 15,200 to 24,800 white cells and from 68 to 77 per cent eosinophiles, but offer no opinion as to etiology or pathology. Stewart[5] reports an interesting case of glandular enlargement, cachexia, and irregular fever in a woman, aged 35, with the white cells ranging from 110,000 to 120,000 and the eosinophiles from 72 to 90 per cent. A study of the post-mortem material in this case revealed lesions consistent with those of Hodgkin's disease. Hay and Evans[6] report a case of acute myelogenous leukæmia with an eosinophilia of 83.7 per cent. Stillman[7] reports a case considered to be one of myeloid leukæmia, showing 91.4 per cent eosinophiles in a white cell count of from 118,000 to 165,000. Giffin[8] contributes a case of a male, aged 31, with an enlarged spleen, liver and axillary nodes. The white count was 15,400, with 66 per cent of eosinophiles. Later, after splenectomy, the white cells increased to 208,000 and the eosinophiles to as high as 90 per cent. The case is not considered as one of leukæmia, but as one of eosinophilic hyperleukocytosis. Shapiro[9] describes a case which he considers to be one of leukæmia, in which the white cells reached 236,000, with 79 per cent eosinophiles. Aubertin and Giroux[10] report a case with repeated attacks of cardiac failure, in which the white cells at one time reached 26,000, and the eosinophiles were found to be present in as high as 68 per cent of the total count. These men regard their case as one of eosinophilia associated with the anoxæmia of cardiac lesions. McDonald and Shaw[11] feel that their case showing 138,000 white cells and 84 per cent of eosinophiles is allied to a true leukæmia. Bass[12] reports a case of a female child of two having slightly enlarged cervical nodes and an enlarged liver and spleen, with 25,600 white cells and 64.8 per cent of eosinophiles. The inguinal and axillary nodes became enlarged before the child died.

DISCUSSION

Following the discovery of the changes in the blood of this patient much debate ensued as to the diagnosis of the disease. Infection with *Trichinella spiralis* was suspected, but no history of pain or tenderness could be elicited from the patient or her relatives, and no tenderness in these parts could be demonstrated. The problem then was to differentiate between Hodgkin's disease and leukæmia of the eosinophilic type. Clinically, the diagnosis of leukæmia was given slight preference to that of Hodgkin's disease because of the generalized glandular enlargement and the blood changes.

Pathologically, the disease is considered to be one of Hodgkin's for the following reasons: (1) the low percentage of myelocytes in the blood; (2) the large numbers of eosinophiles in the bone marrow, only a small number of myelocytes being present amongst them; (3) the fibrosis present about the lymph nodes, especially those in the retro-peritoneal region, where the aorta is partially constricted; (4) the alteration in the architecture of the lymph nodes as noted, *viz.*, a diffuse reticulo-endothelial cell proliferation, the presence of Sternberg giant cells, a variable amount of fibrosis,

and the great increase in the reticular structure, and the diffuse eosinophilic infiltration.

Our thanks are due to Dr. C. P. Howard for allowing us to report the clinical features of this case, and for many valuable suggestions.

BIBLIOGRAPHY

1. LINCOLN, M., *Boston M. & S. J.*, 1908, **158:** 677.
2. SANGUINETTI, H. M., *West Lond. Med. J.*, 1929, **34:** 96.
3. WEBER, F. P., *Medical Press*, 1927, **124:** 152.
4. ALLEN, W. H. AND THRO, W. H., *The Military Surgeon*, 1931, **68:** 503.
5. STEWART, S. G., *Arch. Int. Med.*, 1929, **44:** 772.
6. HAY, J. AND EVANS, W. H., *Quart. J. Med.*, 1929, **22:** 167.
7. STILLMAN, R. G., *Med. Record*, 1912, **81:** 594.
8. GIFFIN, H. Z., *Am. J. M. Sc.*, N.S., 1919, **158:** 618.
9. SHAPIRO, L. G., *Proc. New York Path. Soc.*, 1919, **19:** 73.
10. AUBERTIN, C. AND GIROUX, L., *Presse Méd.*, Paris, 1921, **29:** 314.
11. MCDONALD, S. AND SHAW, A. F. B., *Brit. M. J.*, 1922, **2:** 966.
12. BASS, M. H., *Am. J. M. Sc.*, N.S., 1925, **170:** 416.

PAROXYSMAL VENTRICULAR TACHYCARDIA COMPLICATING COMPLETE HEART BLOCK

(WITH REPORT OF A CASE)

BY G. F. STRONG, M.D.,

Vancouver

THE syncopal and convulsive attacks that so often occur in a case of complete heart block have been usually ascribed to ventricular standstill or asystole. In the past ten years a few instances have been reported in which these seizures in heart block have been accompanied by paroxysms of increased ventricular activity. These have usually been called ventricular fibrillation, but careful analysis of some of them reveals a mechanism more nearly resembling paroxysmal ventricular tachycardia. In some of the reported cases this arrhythmia developed after the use of large doses of quinidine, with and without digitalis. In the case reported here the paroxysms of ventricular tachycardia developed in an established case of complete heart block in which neither quinidine nor digitalis had been administered.

Kerr and Bender[1] reported a case of paroxysmal ventricular fibrillation with cardiac recovery in a case of auricular fibrillation and complete heart block while under treatment with quinidine sulphate. Levine and Matton[2] discussed a case of Adams-Stokes' syndrome showing ventricular fibrillation and asystole, though they point out that the paroxysm resembled ventricular tachycardia. The patient was unconscious and there were no palpable pulse or audible heart sounds during the attack. Davis and Sprague[3] report an instance of paroxysmal ventricular fibrillation occurring after digitalization and the use of large doses of quinidine in a case of rheumatic heart disease with decompensation. Schwartz[4, 5] has reported two cases of the occurrence of transient ventricular fibrillation in complete heart block, and he is of the opinion that this mechanism may account for the syncopal attacks in complete heart block more frequently than has been supposed. Careful analysis of the electrocardiograms in his cases suggests that paroxysmal ventricular tachycardia is an equally suitable designation, though it must be admitted that it is an academic distinction. The second of his cases survived for eight months, with recurring attacks during that time, and to my mind the diagnosis of ventricular fibrillation is not compatible with such a long period. Often the diagnosis of ventricular fibrillation is based on slight irregularity in the rhythm during these paroxysms. Levine and the writer[6] pointed out ten years ago that in ventricular tachycardia the rhythm is usually slightly irregular. In the case to be reported here there is only such irregularity as might therefore be expected.

CASE REPORT

The patient was a private case in the service of Dr. F. N. Robertson, who has kindly supplied the following brief case report.

"Mrs. F., housewife, aged 53, was admitted to Vancouver General Hospital on January 23, 1933, at 8 a.m. and died the same day at 7 p.m.

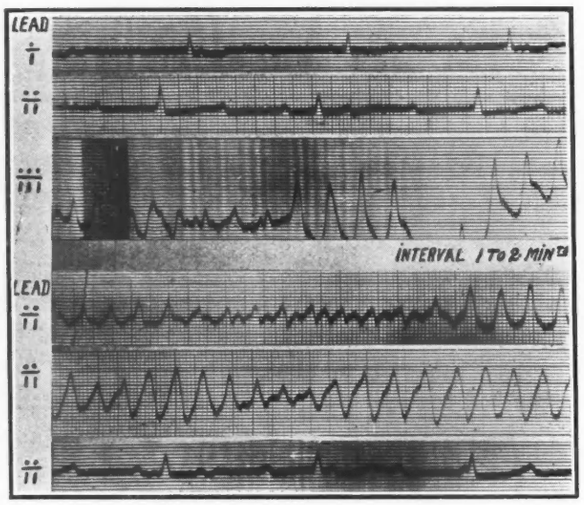
Previous history.—Entirely negative as to rheumatic or other infections.

Present illness.—In March, 1932, she had had a thyroidectomy in another city. She evidently had had some heart trouble before that time, as she was seen by a heart specialist and an electrocardiogram taken. She said her pulse rate was 30 the day of the operation. After that she slowly regained her health, the pulse rate rose, and on numerous occasions was 72.

In September, 1932, she was first seen by me. She complained of faintness and dizziness on exertion. The pulse rate was 36. She was in bed for 7 weeks, taking strychnine and atropine. The pulse was never faster than 44, and usually from 30 to 36. She gradually got up and about, and seemed to have a complete heart

block, with a pulse of 36. She felt perfectly well unless she exerted herself, when she became dyspnœic. Physical and laboratory examinations were otherwise negative.

On January 23, 1933, she awakened at 4.30 a.m., feeling faint, and had a slight convulsion. She had three such seizures before 6 a.m., when I saw her. On examination then her pulse and heart rate were 36, but while listening to the heart it suddenly developed a very rapid rate, uncountable, with just a roaring sound, and the pulse became extremely rapid and small. Just as suddenly this attack subsided, the heart resumed its slow rate, and at this point she went into a mild convulsion for about half a minute. Blood pressure was 180/80. She was sent into hospital where an electrocardiogram was obtained. She was then put on quinidine sulphate, 6 grains every 4 hours. By 5.30 p.m. she had had two doses of quinidine. The attacks were not so frequent, but more severe, and she had typical tonic seizures. She did not come out of them so quickly,



and seemed dazed until the next attack. The last few were exceedingly severe and she became deeply cyanosed. She died in an attack at 7.05 p.m. Permission for an autopsy was refused.''

These electrocardiograms were taken on the old style Cambridge instrument on a 5 by 7 film. The cardiogram was commenced in the usual way at 11 a.m. on January 23rd. When the third lead was started the patient developed another paroxysm of tachycardia, with the onset of which there were some convulsive movements. This lead was taken, the film changed as quickly as possible, and the second film taken with lead II in all three strips. The duration of the paroxysm was between 2 and 3 minutes. The patient was extremely ill even at this time and died 8 hours after the tracing was taken.

The electrocardiogram reveals a complete heart block, the auricular rate being 90 and the ventricular rate 35. On first examination the attack was considered to be ventricular fibrillation, but when the tracing was studied more carefully with calipers there was found only a slight degree of irregularity. The considerable movement of the fibre shown in the third lead is due to the activity of the patient at this point. White[7] has pointed out that there is no sharp line between ventricular tachycardia and ventricular fibrillation. In my opinion the present case is one in which the attacks developed first as paroxysms of ventricular tachycardia and later developed an increasing degree of arrhythmia with subsequent ventricular fibrillation and death. In this patient there were not the syncopal attacks typical of the Adams-Stokes' syndrome. Any loss of consciousness was momentary until the latter part of the day, when the attacks became more severe in character and definite convulsions occurred. During the attack shown in the cardiogram the pulse was palpable, though uncountable because of the extreme rapidity (200), and there was stethoscopic evidence of cardiac activity.

From observations made on other cases of Adams-Stokes' syndrome during the syncopal attacks I cannot feel that paroxysmal acceleration of ventricular activity is a common cause of the loss of consciousness in this condition, though it may occasionally produce that effect.

REFERENCES

1. KERR, W. J. AND BENDER, W. L., *Heart*, 1922, **9:** 269.
2. LEVINE, G. A. AND MATTON, M., *Heart*, 1925, **12:** 271.
3. DAVIS, D. AND SPRAGUE, H. B., *Am. Heart J.*, 1929, **4:** 559.
4. SCHWARTZ, S. P., *Arch. Int. Med.*, 1932, **49:** 282.
5. SCHWARTZ, S. P. AND JEZER, A., *Arch. Int. Med.*, 1932, **50:** 450.
6. STRONG, G. F. AND LEVINE, S. A., *Heart*, 1922, **10:** 125.
7. WHITE, P. D., Heart Disease, Macmillan, Toronto, 1931, p. 665.

VACCINATION AGAINST WHOOPING COUGH.—Thorvald Madsen, Copenhagen, states that the vaccine used in the State Serum Institute in Copenhagen is always made from several recently cultivated strains of Bordet-Gengou bacilli; forty-eight hour blood agar cultures are emulsified in physiological solution of sodium chloride containing 1 per cent solution of formaldehyde, so that the suspension contains about 10,000 millions of bacilli per cubic centimetre. The vaccine is given in three injections intramuscularly or subcutaneously with intervals of from three to four days: 0.5, 0.7 and 1.0 c.c. This dosage is greater than that usually employed. The author believes that the reason for the difference of opinion concerning the value of the vaccination lies to some extent probably in the fact that no sufficient distinction has been made between the therapeutic and the prophylactic properties of the vaccine. Most of the reports conclude that if given early in the catarrhal stage the vaccine will have a good effect. This appears from the reports of most of the Danish officers of health. The greatest difficulty in the appraisal of the effect of whooping cough vaccination is that no suitable control material is at hand. During two epidemics in the Faröe Islands, where suitable control material was available, the mortality in the vaccinatel group was one-sixteenth of that in the non-vaccinated group. This figure is sufficiently large to prove the usefulness of the vaccination when carried out in time. Furthermore, the disease in vaccinated persons takes a much milder course and is of shorter duration.—*J. Am. M. Ass.*, 1933, **101:** 187.

PAPILLARY GROWTHS OF THE RENAL PELVIS*

By David W. MacKenzie, M.D.,

Montreal

IN a study of several reports on renal tumours one finds that intrapelvic growths on the whole are relatively infrequent. Their incidence varies anywhere from 1 to 18 per cent. It is estimated, however, that on an average the pelvic tumours comprise about 5 to 7 per cent of all renal growths. It is rather surprising to find records showing much higher proportions. Thomson-Walker,[4] for example, found 12 cases of tumour of the pelvis in a personal series of 66 renal growths. Hyman[3] also reports a rather high incidence. He found 9 cases of papillary carcinoma of the renal pelvis in a series of 99 kidney tumours. On the other hand, there is in a number of series an incidence of only 1 to 2 per cent. Take our own group of renal tumours; only 2 were papillary growths of the renal pelvis out of a series of 98 kidney growths which consisted of:

Cysts of the kidney (including congenital cystic kidney)	10
Fibroma	2
Adenoma	1
Hæmangioma	2
Sarcoma	3
Leiomyosarcoma	1
Leiomyoma	1
Hypernephroma	21
Cystadenoma papilliferum malignum	2
Carcinoma	53
Papillary carcinoma of the renal pelvis	2

Of course we have had cases of renal growths that may have originated from the renal pelvis, but they have been doubtful, and as a result have not been considered pelvic tumours. It is just possible that some of the cases that have been reported as true pelvic tumours may not have taken their origin from the renal pelvis. We allude to a series of seven cases of growths of the renal pelvis that have been reported by Herman and Greene[1] in 1929. Cases 3, 6 and 7 are not definitely of pelvic origin. The authors themselves suggest that Case 3 is "possibly a primary papillary neoplasm of the pelvis"; that Case 6 is "an extensive renal carcinoma, probably of pelvic origin," and that Case 7 is "a papillary carcinoma of the left kidney."

There is no doubt that at times it is quite difficult to tell the point of origin of a papillary growth that is projecting into the pelvis. Hertzler[2] mentions two cases which seemed definitely to be pelvic, but which were proved to originate in the kidney parenchyma. These so-called papillary carcinomas of the kidney tissue are not true papillary tumours, and although they sometimes simulate a true growth of the renal pelvis yet they really originate from the tubules of the kidney. Papillary growths represent about 70 to 80 per cent of all tumours of the renal pelvis. Of these 60 to 70 per cent are benign, and 30 to 40 per cent are malignant. Several of them are on the border line. The papillary growths of the renal pelvis are similar to the papillary growths of the bladder. They appear alike, they have the same characteristic property of forming transplants, and they simulate each other in their low-grade malignancy.

The pathology of these tumours is rather interesting, and, as we have mentioned above, has the same characteristics as in similar growths of the bladder. The simple papillomata are usually multiple, and appear as villous or wart-like growths. When placed in water they become somewhat branched and elongated, and resemble seaweed very closely. Occasionally the growth has an extensive distribution and may involve the ureter, the bladder, and even the ureter on the opposite side. Often there is one large growth and several smaller ones surrounding it. Frequently these growths are associated with salty incrustations and even with definite calculi. These papillomata are all very vascular and bleed easily. This accounts for the marked hæmaturia that is usually the outstanding symptom in the disease. Microscopically the picture is typical. The structure of the papilloma is simple and uniform. It consists of a series of branching clusters of stroma covered by many layers of transitional epithelium. The stroma is usually made up of fine, branching blood vessels which are in close association with some connective-

* Read before the International Urological Congress, London, July, 1933.

tissue and smooth-muscle fibres. The tumour cells are cubical, cylindrical, or even elongated, and round-cell infiltration is present. The base of the growth is free from any invasion of the essential tumour cell.

These growths are benign, but have a tendency, like the simple papillomata of the bladder, to become malignant. They do not metastasize but possess the quality of producing transplants along the ureter and in the bladder. The malignant papillomata are also wart-like or cauliflower in character, but appear more compact and involve usually a greater area than the simple papillomata. At times the entire kidney is replaced by growth. The villous processes are not as long or branching, and very often show areas of ulceration. Here too the growth may extend downwards to involve the ureter and the bladder. In the early stages there is definite evidence of involvement of the submucosa, and later the renal parenchyma is encroached upon. In advanced cases there is usually distension of the renal pelvis and the presence of multiple cysts in the cortex of the kidneys. These tumours are also extremely vascular and bleed very easily. Microscopically, the essential tumour cells are found to have invaded the base of the growth and the submucosa. In some growths one finds areas showing benign and malignant cells side by side, suggesting a transformation from a benign to a malignant state.

The two cases that we have referred to above belong to the group of papillary carcinoma. The following is a brief summary of each report.

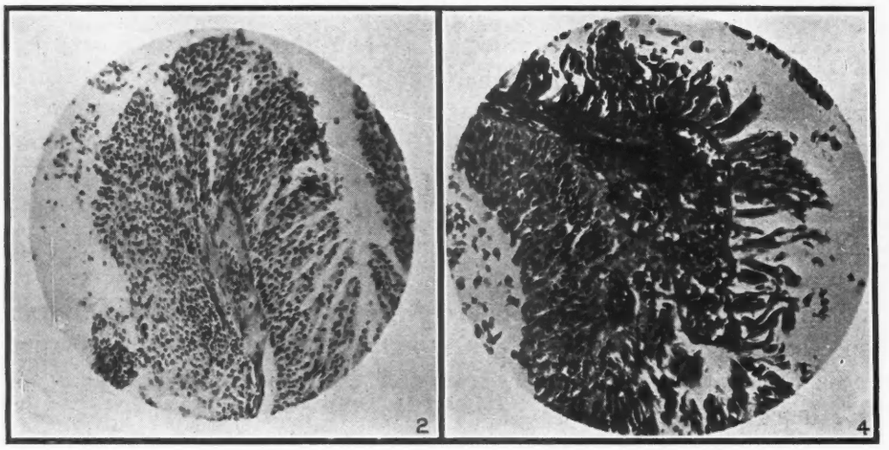


FIG. 1.—*Case 1.* Note the large cauliflower-like papillary growth which has replaced about two-thirds of the kidney. Note also the large cyst which has been cut across.

FIG. 2.—*Case 1* (high power). Showing one papillary projection. Note the many layers of stratified transitional epithelium.

FIG. 3.—*Case 2.* Note a small papillary growth involving the upper part of the pelvis, also the compression of the medulla and cortex in this area, with formation of a cyst.

FIG. 4.—*Case 2* (high power). Showing one papillary projection which consists of a fibrous stalk and many layers of stratified transitional epithelium.

CASE 1

(No. 9896) A male, aged 52, who gave a history of hæmaturia which was first noticed ten years prior to admission. He then had some hæmaturia off and on until he came to the hospital. After a thorough examination a diagnosis of tumour of the right kidney was made and a nephrectomy and ureterectomy were performed.

The specimen consisted of a kidney about three times the normal size, the upper two-thirds of which was completely replaced by a papilliferous, somewhat cystic, growth having a distinctly cauliflower-like appearance (Fig. 1). The parenchyma of the lower pole was pale, swollen, with loss of normal markings. Microscopically, the sections showed the growth to consist for the most part of fibrous stalks surmounted by layers of stratified transitional epithelium, simulating the papillary growths met with in the bladder (Fig. 2). In some areas the papillary structure was aborted and more or less direct invasion with compression of the renal parenchyma had occurred. There was a distinct tendency however for the cells to remain narrow, elongated, and piled upon each other, as in the papillary portion. The kidney parenchyma showed profuse exudative and productive inflammation. *Anatomical summary.* — Papillary carcinoma of the renal pelvis involving the parenchyma of the kidney.

Case 2

(No. 10927) A male, aged 71, who gave a history of hæmaturia and the passage of small pieces of tissue in his urine off and on for two years. A diagnosis of malignant growth of the right kidney was made, and the patient was subjected to a nephrectomy and ureterectomy.

The specimen was that of a kidney slightly larger than normal and covered with some dilated veins. There was no evidence of growth on the outside. Split open a papillary growth was present, which involved the upper part of the pelvis (Fig. 3). This growth appeared well demarcated, but had compressed the medulla and the cortex in this area with the formation of a filbert-sized cyst. The remaining portion of the kidney showed considerable peri-pelvic fat and definite markings of coarse irregular lobation under the capsule. Microscopically, the sections showed a papillomatous growth of stratified transitional cells, similar to that met with in the bladder, which had apparently originated in the pelvis of the kidney (Fig. 4). It had invaded the parenchyma, which was compressed and, while fairly well demarcated, showed evidence of malignant infiltration. Section taken through the small pinhead greyish nodule in the cortex showed it to consist of growth similar to that described above. There was also considerable metastatic involvement in the cortex in this area. *Anatomical summary.*—Transitional-celled papilloma of the renal pelvis which has become cancerous.

It is of interest to note that both these patients have been well and free from recurrence for almost two years. In each case only a nephrectomy and a partial ureterectomy had been performed.

Metastases from papillary carcinoma of the renal pelvis like those from growths of the bladder occur quite late. They have, however, the inherent quality of spreading and forming transplants. This often results in very extensive growths involving the kidney parenchyma, the ureter, the bladder and even the ureter on the opposite side. Metastases have been found in the adrenals, peritoneum, liver, lungs, bones and lymph nodes.

A few words must be said regarding the diagnosis of papillary growths of the renal pelvis. A great deal has been written discussing the methods used to properly diagnose the condition. After all, there are no signs, symptoms or clinical findings that are pathognomonic of a growth of the renal pelvis. A tumour of the renal parenchyma will give you the same clinical picture. Therefore, in order to arrive at a possible diagnosis all available data are to be studied. The history, physical findings, urinary studies, and finally cystoscopy with pyelography are all essential. I must mention one clinical finding that to my mind is perhaps of more value than any of the other data. I refer to the history that some patients give of passing pieces of tissue in the urine. Microscopic examination of these specimens reveals papillomatous structure. Of course that may be due to growth in the bladder, but if on cystoscopy the bladder is found to be free from growth then a tumour of the renal pelvis must be seriously considered. Such a history was given by Case 2. His family doctor, who referred him to us, had the pieces of tissue examined and a diagnosis of papilloma of the bladder was made. His bladder was and is still absolutely free from growth.

There is one other important point that I wish to refer to. If one encounters a vesical growth which is situated near or around the ureteral orifice, the corresponding kidney and ureter must be investigated. As we mentioned above, vesical and ureteral transplants from a growth in the renal pelvis are not uncommon, and therefore that possibility is to be ruled out.

References

1. Herman and Greene, *Ann. Surg.*, 1929, **89**: 682.
2. Hertzler, Surgical Pathology of the Genito-Urinary Tract, Lippincott, Phila., 1931.
3. Hyman, *Am. J. Surg.*, 1928, **5**: 120.
4. Thomson-Walker, *Brit. J. Urol.*, 1929, **1**: 141.

Doctors and Hospital Patients.—The relationship of doctors to their patients in the hospital is one of importance. Because a person is ill and in a hospital is no reason for other than the most courteous attention and the use of polite language. In the public ward among the poor, and in the private ward beside the bed of the rich, the same ideals of refined deportment should ever be present. The rich patient need not be flattered and the poor patient should not be humiliated. A cheerful and kindly manner to both will aid materially in hastening recovery, and lessening the weight of sickness and pain. The requests of patients must at times be refused, but this can be done in such a way as to make them realize that the refusal is for the benefit of the one refused. The Latin maxim *Suaviter in modo et fortiter in re*, pleasant in manner but firm in purpose, puts the course that should be adopted in clear and terse form. Tact is everything. It is not a sixth sense, but it is like the life of all the five. It is the open eye, the quick ear, the judging taste, the keen smell, and lively touch; it is the interpreter of all riddles, the surmounter of all difficulties, the remover of all obstacles. Above all things cultivate tact, for it knows what to do.—Bulletin No. 7 of the Canadian Hospital Council "Relations Between the Medical Staff and the Hospital".

BILIRUBIN FORMATION AND THE RETICULO-ENDOTHELIAL SYSTEM*

III. FUNCTIONAL BLOCK OF THE RETICULO-ENDOTHELIAL SYSTEM

BY R. GOTTLIEB, M.Sc., M.D.,

Montreal

WE have been able to show so far that the Kupffer cells of the liver are real cellular elements and not mere thickenings of an endothelial lining of the sinusoids, which in reality hardly exists.[1] We also demonstrated that the reticulo-endothelial cells can be at least temporarily blocked.[2] The evidence however was entirely anatomical, and it still remained to prove that it is also possible to produce a functional block of the reticulo-endothelial system. If after a complete block of this system the formation of bilirubin should cease the final proof for the formation of bilirubin by the reticulo-endothelial system would be established.

We have attempted to prove the functional block of the reticulo-endothelial system in two ways:

1. The effect of toluylenediamine poisoning, which produces a hæmolytic jaundice, was studied in normal rats and then compared with the effect produced in rats in which the reticulo-endothelial system was blocked by means of thorium dioxide.

2. The bilirubin content of bile obtained from dogs with biliary fistulas was compared with the bilirubin content of the bile of the same animals after they had been injected with large amounts of thorium dioxide, which can produce a block of the reticulo-endothelial system, as we were able to demonstrate histologically.

1. TOLUYLENEDIAMINE POISONING

Sixteen normal rats were injected with 0.5 c.c. of a 10 per cent aqueous solution of toluylenediamine intraperitoneally. Blood was taken from these animals, which showed signs of toxicity (apathy, lack of appetite), 24 hours after the injection, and the bilirubin-content estimated by the van den Bergh test. In all the animals the van den Bergh reaction was negative prior to the poisoning. Twenty-four hours after the poisoning an indirect positive van den

* From the Department of Medicine, McGill University Clinic, Royal Victoria Hospital, Montreal.

This research was made possible by a grant from the Banting Research Foundation.

TABLE I.

Animal Number	*Bilirubinæmia after Toluylenediamene Poisoning mgrm. /100 c.c.*	*Red Blood Cells prior to Poisoning*	*Red Blood Cells after the Poisoning*	*Remarks*
1	0.75	7,600,000	5,200,000	
2	1.00	7,200,000	4,900,000	
3	1.5	7,800,000	5,600,000	
4	....	7,900,000	.....	Animal died 10 hours after injection.
5	1.5	8,100,000	5,600,000	
6	1	7,300,000	5,000,000	
7	....	7,200,000	.....	Animal died 6 hours after injection.
8	0.75	8,000,000	5,100,000	
9	....	7,600,000	.....	Animal died 14 hours after injection.
10	1.00	7,700,000	4,900,000	
11	1.00	7,300,000	4,800,000	
12	....	7,500,000	.....	Animal died 18 hours after injection.
13	1.5	7,600,000	5,100,000	
14	1	7,600,000	5,200,000	
15	1.5	8,000,000	5,100,000	
16	1.5	7,500,000	4,900,000	
Average	1.162	7,600,000	5,100,000	

Bergh reaction was found in all animals in which the blood could be examined (4 rats died before the blood could be taken). The average amount of bilirubin after the poisoning was found to be 1.162 mgrm. in 100 c.c. The erythrocytes, which were counted before and after the poisoning, came down from an average of 7,600,000 to an average of 5,100,000. (See Table I).

Thirty rats which had been previously injected with varying amounts of thorium dioxide in a 25 per cent colloidal suspension were then poisoned in the same way with toluylenediamine. It was found that those rats which had only small doses of thorium dioxide responded to the toluylenediamine in exactly the same way as the normal animals. That is, of 6 rats which had received 0.5 c.c. of thorium dioxide twenty-four hours before the poisoning, 5 showed twenty-four hours after the poisoning an average bilirubinæmia of 1.15 mgm. in 100 c.c.; one rat died before the blood could be taken. Six rats which received 1 c.c. of thorium dioxide twenty-four hours prior to the poisoning showed similar results twenty-four hours after the toluylenediamine injection, the average amount of bilirubin in the blood being 1 mgm. in 100 c.c. In the animals in which the dose of thorium dioxide was further increased no bilirubinæmia was produced. Three out of 6 animals which had received 1.5 c.c. of thorium dioxide showed only a trace of bilirubin; one animal died before the blood could be taken; while 2 showed no bilirubin in the blood at all after poisoning with toluylenediamine. Six rats were injected with 2 c.c. and 6 with 3 c.c. of thorium dioxide twenty-four hours prior to the poisoning. Eleven of these rats did not develop a bilirubinæmia; one animal died before the blood could be taken. The erythrocytes were markedly diminished in all animals after the poisoning. The average count of 7,600,000 prior to the poisoning diminished to an average of 4,900,000, twenty-four hours after the poisoning. (See Table II).

TABLE II.

Animal Number	*Amount of Thorium Dioxide Injected in c.c.*	*Bilirubinæmia after Toluylenediamene Poisoning mgrm. /100 c.c.*	*Red Blood Cells prior to Poisoning*	*Red Blood Cells after the Poisoning*	*Remarks*
17	0.5	1.5	7,300,000	4,800,000	
18	0.5	0.75	7,600,000	5,000,000	
19	0.5	1.00	8,100,000	4,900,000	
20	0.5	....	7,700,000	.....	Animal died 6 hours after poisoning.
21	0.5	1.00	7,400,000	5,100,000	
22	0.5	1.5	7,500,000	4,900,000	
23	1	1.5	7,300,000	4,800,000	
24	1	0.75	7,800,000	5,000,000	
25	1	1.00	8,200,000	5,100,000	
26	1	1.00	8,000,000	4,600,000	
27	1	0.75	7,600,000	4,700,000	
28	1	1.00	7,900,000	4,500,000	
29	1.5	0	7,500,000	5,300,000	
30	1.5	trace	8,100,000	5,100,000	
31	1.5	trace	8,000,000	4,900,000	
32	1.5	0	8,200,000	5 100,000	
33	1.5	....	7,900,000	.....	Animal died 18 hours after poisoning.
34	1.5	trace	7,900,000	4,900,000	
35	2	0	8,100,000	5,000 000	
36	2	0	7,200,000	4,600,000	
37	2	0	7,600,000	4,900,000	
38	2	0	8,000,000	4,800,000	
39	2	0	7,700,000	4,900,000	
40	2	0	7,800,000	5,000,000	
41	3	0	7,100,000	4,600,000	
42	3	....	7,300,000	.....	Animal died 22 hours after poisoning.
43	3	0	7,500,000	4,700,000	
44	3	0	7,900,000	5,200,000	
45	3	0	7,400,000	5,100,000	
46	3	0	7,300,000	4,900,000	
Average			7,600,000	4,900,000	

2. Blocking of the Reticulo-Endothelial System of Dogs With Biliary Fistulas

Biliary fistulas were made in dogs and the animals standardized; the method of Rous and McMaster,[3] which makes it possible to obtain sterile bile, was used. After standardization the animals were injected with a blocking dose of thorium dioxide. While the rats were found to be very little or not at all affected by the thorium dioxide, the dogs were much less resistant and died a few hours after the injection of the total blocking dose. Eventually we succeeded, after dividing the total dose into two injections, twenty-four hours apart, in having three dogs survive this procedure; one lived 3 days, one lived 6 days, and one 10 days after the last injection. The total blocking dose was found to be 6 c.c. of the 25 per cent colloidal suspension of thorium dioxide per kilo of body weight. Charts 1, 2, and 3 show the detailed results.

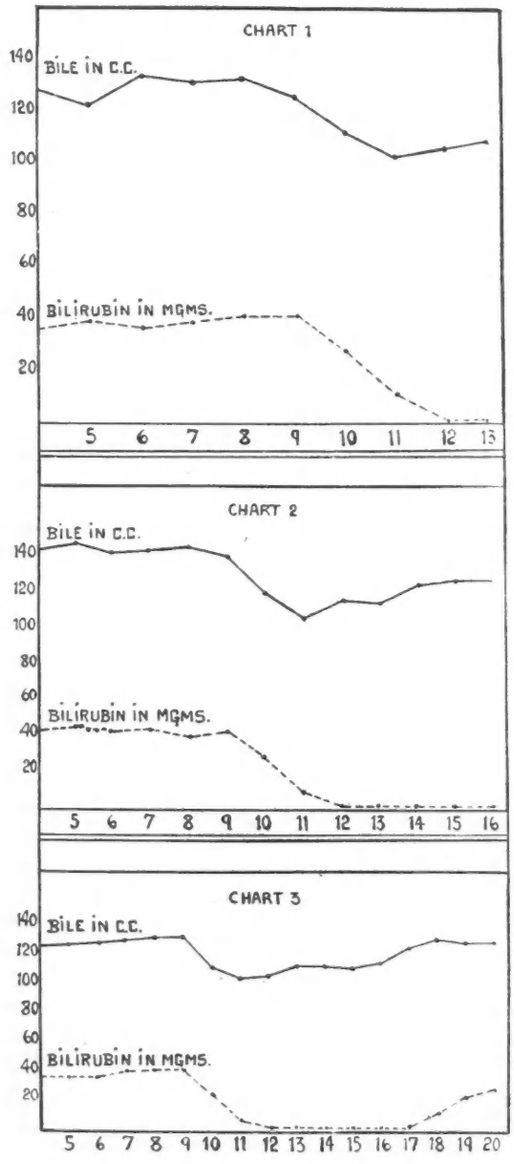


CHART 1.—Dog No. 4; weight 8 kilos; 13 days of biliary fistula; 24 c.c. THO_2 intravenously on the 9th day; 24 c.c. THO_2 intravenously on the 10th day.

CHART 2.—Dog No. 6; weight 9 kilos; 16 days of biliary fistula; 26 c.c. THO_2 intravenously on the 9th day; 26 c.c. THO_2 intravenously on the 10th day.

CHART 3.—Dog No. 9; weight 8½ kilos; 20 days of biliary fistula; 25 c.c. THO_2 intravenously on the 9th day; 25 c.c. THO_2 intravenously on the 10th day.

The experiments were conducted as follows. For three days after the operation the animals were left alone. After three days the bag of the fistula was for the first time opened and emptied; the bile which had accumulated during these days was discarded. The bag of the fistula was then emptied every twenty-four hours. All manipulations were carried out with the strictest aseptic precautions. The total daily amount of bile was measured and the amount of bilirubin estimated by Hooper and Whipple's method.[4] When the amount of bile and bilirubin was found to be constant for five days, the first injection of thorium dioxide was given, and twenty-four hours afterwards the second dose. The total amount of bile and bilirubin was measured every twenty-four hours. The total amount of bile only diminished slightly after the thorium dioxide injection, while the bilirubin disappeared entirely within forty-eight hours after the second injection. Only one animal lived long enough (dog No. 9, see Chart 3) to show a return of the bilirubin in the bile. At autopsy pneumonia was found to be the cause of death in all three animals.

Discussion

The experiments with toluylenediamine poisoning as well as the studies on the dogs with biliary fistulas show that it is possible to produce a functional block of the reticulo-endothelial system. Although it is evident that this block is only a temporary one, it persists long enough to judge the function of the system so far as bilirubin formation is concerned. It is in the nature of the reticulo-endothelial system to proliferate whenever an increased demand is made upon it, and it is therefore only to be expected that the block would be temporary. The fact, however, that while the block of the reticulo-endothelial system is established bilirubin formation ceases proves in our opinion that bilirubin is

formed in the reticulo-endothelial system. The questions arise now as to what organs can produce bilirubin, and whether we can still speak of hepatic or extra-hepatic bilirubin formation. Man, Sheard, and Bollman[5] have shown, by comparing the bilirubin content of the arterial and venous blood of the spleen, liver, and bone marrow, that bilirubin is formed in these organs. Since the reticulo-endothelial system is distributed practically throughout the whole organism, we assume that at least at certain times all these seats of reticulo-endothelial elements may assume the formation of bilirubin. The liver with its Kupffer cells contains a certain amount of the reticulo-endothelial system and takes, therefore, part in bilirubin formation, but only to a small extent. The liver *per se* is not essential in the formation of bilirubin; it is its "splenic portion" which participates in the bilirubin formation. The liver parenchyma may be essential for the production of the final whole bile (bile salts, etc.), and may alter the bilirubin at its passage, but has nothing to do with the actual bilirubin-formation itself. We believe, therefore, that bilirubin is formed extrahepatically, while the hepatic bilirubin is insignificant, and the term, being misleading, should be dropped.

Rosenthal and Melchior[6] have put forward the view that reticulo-endothelial cells merely act as phagocytes of bilirubin formed elsewhere. Bieling and Isaac[7] suggest that bilirubin is formed extra-cellularly by the aid of some enzymes. The experiments of Rich[8] and coworkers show however quite clearly that the formation of hæmatoidin in blood extravasates is entirely dependant upon the presence of wandering endothelial cells around the clot. Rich[9] was able to show that only mesodermal and not ecto- or endo-dermal cells can transform hæmoglobin into bile pigment.

CONCLUSIONS

From the experiments detailed above we believe that:

1. Complete block of the reticulo-endothelial system leads to cessation of bilirubin formation. The reticulo-endothelial system is therefore essential for bilirubin formation.

2. "Hepatic bilirubin" formation is limited to the reticulo-endothelial portion of the liver (Kupffer cells) and this term should be dropped as misleading.

I wish to express my sincerest thanks to Dr. H. Doubilet, of the Department of Experimental Surgery, for his active help and advice in obtaining the biliary fistulas in our animals.

REFERENCES

1. GOTTLIEB, R., *Canad. M. Ass. J.*, 1934, **30:** 256.
2. GOTTLIEB, R., *Ibid.*, 1934, **30:** 365.
3. ROUS, P. AND MCMASTER, P. D., *J. Exp. Med.*, 1923, **37:** 11.
4. HOOPER AND WHIPPLE, *Am. J. Physiol.*, 1916, **40:** 332.
5. MANN, F. C., SHEARD, C. AND BOLLMAN, J. L., *Am. J. Physiol*, 1926, **78:** 384.
6. ROSENTHAL, R. AND MELCHIOR, E., *Arch. f. exp. Path. u. Pharm.*, 1921, **98:** 28.
7. BIELING, R. AND ISAAC, S., *Ztschr. f. d. ges. exp. Med.*, 1921, **25:** 1; *Ibid.*, 1922, **26:** 251; 1922, **28:** 154 and 180.
8. RICH, A. R. AND BUMSTEAD, J. H., *Bull. Johns Hopk. Hosp.*, 1925, **36:** 437.
9. RICH, A. R., *Bull. Johns Hopk. Hosp.*, 1925, **35:** 415.

UNDULANT FEVER: ITS RELATION TO BRUCELLIASIS IN DOMESTIC ANIMALS.—In order to emphasize the close association of brucelliasis in animals and man, L. E. Starr presents a short review of the results of early investigations. For the diagnosis of undulant fever in man and brucelliasis in animals, the agglutination and the complement fixation tests are most commonly used. Although they compare favourably in accuracy, the agglutination test is generally used on account of its comparative simplicity. This test, when set up and interpreted by experienced men, is as reliable as any serological test in use today. The occurrence of active infection and clinical disease following exposure is largely dependent on four major factors: (1) the portal of entry, (2) the virulence of the particular strain or strains of the organism involved, (3) the number of organisms and (4) the resistance of the host. Brucella infection in the human being apparently follows the same course in the body as in animals, as evidenced by frequent involvement of the reproductive tract. The periodic functioning of the mammary gland and other peculiarities of the host or of the infective organism not thoroughly understood probably preclude the gland acting as a permanent reservoir of infection. At the time of abortion or normal pregnancy in the case of infected cattle, hogs and goats, the organism is thrown off in myriad numbers with the fetus, placenta, amniotic fluid, and subsequent uterine discharges. Human Brucella infection originating from swine has been shown to be relatively common in those states in which swine are raised extensively. Undulant fever in man may be classified in part as the result of occupational hazards and in part from ingestion of raw contaminated dairy products. Epidemiological data collected by various investigators indicate that approximately 40 per cent of the cases of undulant fever occur among people employed on farms. Although the disease is primarily one of late adolescence and adult life, infants and aged people are occasionally affected. The geographic location of the cases in Virginia indicates the close relationship of undulant fever with Brucella infection in cattle. Brucella infection is primarily a disease of animals. Of the domestic animals only goats, cattle, hogs and possibly horses are of importance in the perpetuation of the disease in nature. Man is accidentally infected either by direct contact with infected animals or their discharges or by the ingestion of raw dairy products from infected dairy cattle or goats. The control and eventual eradication of undulant fever in man is dependent entirely on the control and eradication of the disease in domestic animals.—*J. Am. M. Ass.*, 1934, **102:** 902.

EPIDERMOID CYST IN BONE*

BY J. H. COUCH, M.B., F.R.C.S.,

Toronto

THE occurrence of an epidermoid cyst within the bone is a rare and anomalous condition. Christopher,[1] Harris,[2] Sonntag,[3] Curtis and Owen,[4] each record a single instance, while Friedländer[5] reports two cases. Thus, only 7 authentic cases, including that which is described in this article, have been found.

Some obvious confusion in the naming of these small cysts indicates the need for a definite statement as to nomenclature, and a brief definition of the various terms used. The cysts under discussion are properly called epidermoid cysts because they are derived from the epidermis and epidermis only. Harris[2] called his tumour a "sebaceous cyst". Curtis and Owen[4] seem to have followed Harris's nomenclature, and also call their tumour "sebaceous cyst". Both authors recognize clearly the pathology underlying this formation and agree that it is not a "sebaceous cyst". Christopher[1] correctly calls his tumour "epidermoid cyst". The German writers, Sonntag[3] and Friedländer,[5] call the cysts which they encountered, "epithelial cysts", which is also correct.

A *sebaceous cyst* is a cyst in the skin arising because of the obstruction of the outlet of a sebaceous or oil gland. The gland continues to secrete sebum or oil within its ramifications and expands behind the obstruction. The content, therefore, is oil or sebum. The wall consists of columnar epithelium which may be flattened by pressure.

An *epidermoid cyst* is the result of inclusion of some epidermal or epithelial cells within the deeper layers of the skin or below the skin. These few cells continue to grow and to proliferate so that the content of epidermoid cysts is degenerated, desquamated, keratinized epithelium and the wall is of stratified epithelium.

A *dermoid cyst* is a cyst containing all layers of the skin or derma and will contain, therefore, all skin appendages such as hair, sweat glands, sebaceous glands, as well as epidermis and the underlying layers of skin. This is defined by Ewing.[6] Dermoids are the result of embryological "rests" or congenital failures at the lines of fusion resulting in the inclusion of the whole thickness of skin. The content, therefore, is desquamated squamous epithelium, sebaceous material, sweat, hair, teeth, nails—all skin appendages.

Teratomatous cysts are closely related to this last group, but may contain evidences of all three embryonic layers, ectoderm, mesoderm, and entoderm, namely, muscle, cartilage, bone, connective tissue, blood vessels, as well as skin appendages.

The present case, in connection with which the theories of etiology are reviewed, offers a typical clinical history which should make possible an accurate pre-operative diagnosis.

CASE REPORT

In the case of Mr. McQ., here cited, the chief complaint was of pain in the left thumb, lasting over a period of two months. Two months before, while grasping a light cardboard shoe box, the patient experienced sharp pain in the terminal phalanx of the left thumb. He continued his work, but a soreness persisted, and he applied to the Welfare Department of his firm. X-ray revealed a cyst in the bone, and he was referred to the Toronto General Hospital. Further diligent questioning elicited the fact that he had struck his left thumb with a hammer thirteen years before. This blow was so forceful that it had "split the nail across".

Examination.—On careful comparison of the injured thumb with its normal fellow of the right side, it was seen to be definitely thicker, and there was a point of maximum tenderness on the medial side, proved to correspond with the site of a fracture sustained undoubtedly while lifting the shoe box.

The x-ray showed a cyst in the bone of the terminal phalanx, with a definite clear-cut wall. The cyst was surrounded by a thin shell of bone, which had been fractured on its medial aspect.

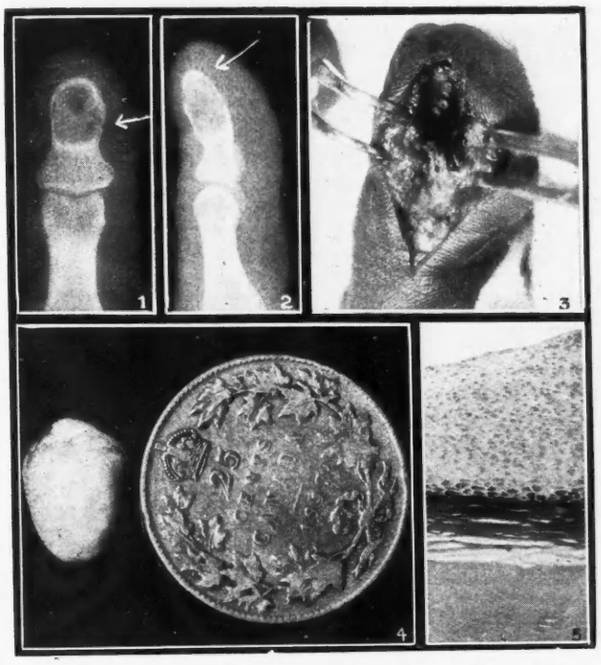
Diagnosis.—The pre-operative diagnosis was "epidermoid cyst in bone", with fracture through the cortex.

Operation.—Under general anæsthesia, and with a tourniquet in place, an incision was made along the side of the thumb. The bone, which was readily exposed, was found to be of an egg-shell thinness and was readily removed, leaving a pearly white, tough-walled cyst which was easily rolled out of its bed by blunt dissection with the back of a needle. A clean smooth walled cavity was left in the bone. The wound was closed without drainage and healed by primary union.

Description of the specimen.—In the gross the specimen consisted of a cyst, measuring 1.0 x 0.75 c.m. It was covered by a tough, white wall and contained thick, grumous material.

* From the Department of Surgery, University of Toronto.

On microscopic examination, the walls of the cyst were seen to be made up of layers of stratified squamous epithelium with keratinization, while the contents proved to be desquamated, degenerated, keratinized cells. The pathologist's diagnosis was "epidermoid cyst".



FIGS. 1 AND 2.—Antero-posterior and lateral skiagrams, to show cyst in bone. Note the fracture.

FIG. 3.—To show smooth hollow in bone at operation.

FIG. 4.—Gross view of cyst; size compared to a quarter.

FIG. 5.—Microscopic view of the cyst wall with desquamated epidermal cells.

Etiology and pathology.—In these cases we are dealing with a cyst of purely ectodermal origin, lying within bone which is a purely mesoblastic structure. There is no communication between the cyst and the skin. Two theories, which may be summarized, have been suggested to account for its appearance in this strange location. The first is that of metaplasia of cells. Can the cells of the three primary embryonic layers, ectoderm, entoderm, mesoderm interchange? This old problem of biology has long been debated and there is still no unanimity of view. It is fruitless to follow the arguments here; suffice it to say that the theory of metaplasia is neglected by most pathologists. The second theory of causation is that of implant by trauma and this seems to be the most acceptable; at some time, the subject has suffered a direct injury, with a punctured wound. A few cells were carried from the epidermis right into the bone, beneath the periosteum, where they grew and produced the cyst. An injury severe enough to carry some cells of the epidermis to the interior of the bone is likely to remain fixed in the mind of the patient. A careful review will usually elicit a history of severe local injury some time in the past. The strongest constructive evidence for the traumatic theory is the location of the cysts. They have been found in the terminal phalanges of the fingers, where repeated crushes and injuries are most common. It is also significant that epidermoid cysts lying in the soft tissue immediately under the skin are found most commonly in the fingers and hands, and these are accepted as being due to implant by trauma.

The *typical clinical picture*, illustrated by the present case may be briefly emphasized. In these epidermoid cysts in bone we have a definite clinical entity. In all cases the history, clinical findings, and x-ray have much in common, and are so characteristic that a definite pre-operative diagnosis can be made. The complaint is characteristically of sudden pain over the terminal phalanx, brought about by slight pressure and coinciding with a fracture of the cortex over the cyst. The tenderness persists. In the history the patient usually recalls a rather severe crushing or puncture injury some time in the past, and on examination the affected part is found to be constantly tender, with one point of maximum tenderness over the fractured cortex. Comparison with the normal side will show a thickening of the phalanx.

X-ray reveals a definite clear-cut, smooth-walled cyst, which produces atrophy and destruction of nearby bone by pressure. The cortex is thin over the cyst and may be lacking on one side. If there is a history of recent sudden pain on slight pressure a fracture through the cortex will be seen. The presence of the cyst produces atrophy of bone so that the phalanx is destroyed, leaving the cyst covered with a thin shell. But it also must stimulate bone production, for the whole phalanx is larger than normal and gives the appearance of having been "expanded" by the cyst; new bone must therefore have been laid down outside, as it was eroded inside.

Treatment.—The most effective treatment is to remove the cyst intact, although Friedländer felt it wise to amputate in both his cases, as also did Sonntag. Removal of the cyst is easily accomplished, for the smooth-walled,

fairly tough cyst simply peels out of its bony bed on blunt dissection and leaves behind a smooth-walled hollow in the bone. The advisability of placing a bone graft in this cavity has been considered, but experience has shown that it is unnecessary if the part be protected from further fracture for three weeks.

If untreated these cysts would progress and destroy the affected part of the phalanx. They would burst through cortex and spread in soft tissue, necessitating amputation.

They respond to treatment and may be cured with no likelihood of recurrence.

SUMMARY

1. A case of epidermoid cyst in the bone is recorded.

2. Cysts arising from epidermal cells occur in bone.

3. Such cysts occur in phalanges.

4. These cysts are the result of traumatic implantation of epidermal cells some time previously.

5. The history, physical findings and x-rays are characteristic, and permit accurate diagnosis.

6. Treatment consists in the removal of the cyst intact.

REFERENCES

1. CHRISTOPHER, *Minn. Med.*, 1925, **8:** 607.
2. HARRIS, *J. Bone & Joint Surg.*, 1930, **12:** 647.
3. SONNTAG, *Münch. med. Wchnschr.*, 1923, **20:** 1055.
4. CURTIS AND OWEN, *J. Bone & Joint Surg.*, 1933, **15:** 998.
5. FRIEDLANDER, *Zentralbl. f. Chir.*, 1930, **57:** 209.
6. EWING, Neoplastic Diseases, Saunders, Phila., 1919, p. 941.

CYANOSIS IN NITROUS OXIDE OXYGEN ANÆSTHESIA IN MAN

BY BERNARD B. RAGINSKY AND WESLEY BOURNE,

Laboratory of Pharmacology, McGill University,

Montreal

THE substitution of an oxygen-nitrous oxide mixture for one of air and nitrous oxide by Andrews[1] in 1869 marked the real beginning of nitrous oxide anæsthesia. This helped to reduce the cyanosis to a great degree, but did not do away with it entirely. Nine years later, Paul Bert[2, 3] subjected some patients to a nitrous oxide-oxygen mixture in a pneumatic chamber under one and one-quarter atmospheres of pressure, using an 85:15 mixture of nitrous oxide and oxygen. He believed that a sufficient concentration of nitrous oxide for anæsthesia and enough oxygen for the prevention or amelioration of the asphyxia could thus be attained.

HISTORICAL

Various experiments have been carried out on laboratory animals to determine the quantities of nitrous oxide and oxygen present in the arterial blood under this type of anæsthesia. In 1873, Jolyet and Blanche[4] found that in a dog under a 62:21 mixture, administered for seven and a half minutes, the arterial blood contained 29 volumes per cent of nitrous oxide. In the same animal, using pure nitrous oxide for one and three-quarter minutes, they found 28.1 volumes per cent of nitrous oxide. In two other dogs, inhalation of the pure gas for three and four minutes, respectively, produced concentrations in the blood of 34.6 and 37 volumes per cent.

Nicloux,[5] carrying out similar experiments in dogs, found that the pure gas administered for two to two and a half minutes produced a nitrous oxide content of the arterial blood of 25 volumes per cent, and, if the anæsthesia were continued, the content rose to as high as 30 volumes per cent just before death. Somewhat similar values have been reported by other investigators. Olivier and Garret[6] found that when complete anæsthesia was induced in the rabbit the nitrous oxide content of the blood was 22.5 volumes per cent.

Kemp[7] analyzed the blood of dogs under nitrous oxide anæsthesia for its oxygen content, and found it to vary between 7.9 and 14.2 volumes per cent. As he did not report the oxygen capacity, no information can be deduced as to the extent of oxygen unsaturation. Using mixtures containing from 88.5 to 93.9 per cent of nitrous oxide, he found the nitrous oxide content of the blood to vary from 29.1 to 33.5 volumes per cent. He states that in full anæsthesia sufficient oxygen is present to maintain consciousness even if no nitrous oxide were present. More recently, Leake and Hertzman,[8] working on dogs and using 90:10 to 85:15 mixtures of the gases, found it impossible to obtain true anæsthesia without some degree of anoxæmia. In their experiments the arterial blood contained from 82.3 to 90.5 volumes per cent of oxygen. Cullen, Austin, Kornblum and Robinson[9] decided that it was impossible to secure anæsthesia in the dog without using 95 per cent or more of nitrous oxide, and that in all these cases anoxæmia was present.

Greene, Currey, Dexheimer, Hannan and Harlan[10] used mixtures of the gases sufficient to produce anæsthesia in dogs and found the concentration of nitrous oxide in the blood to range from 20.6 to 26.6 volumes per cent, with an average of 23.3. The deviations from the average saturation bore no relation to the degree of anæsthesia. They observed the arterial oxygen to vary through a wide range — from 2.1 to 18.8 volumes per cent. In their experiments the oxygen saturation ranged from 11 to 70 volumes per cent. The depth of anæsthesia was inversely proportional to the concentration of oxygen present in the blood. These oxygen concentrations are much lower than those found by Leake and Hertzman. Using the latter's criterion of anoxæmia (oxygen saturation below 92 per cent), these animals were markedly anoxæmic. The

difference in the results may be explained partly by the fact that the anæsthesia induced by Greene and his co-workers may have been deeper than that obtained by Leake and Hertzman.

Recently, Brown, Lucas and Henderson[11] have repeated the experiments of Bert upon rabbits and cats, using pressures of from one and one-quarter to two atmospheres and oxygen percentages of from 5 to 21. They found that so long as the partial pressure of oxygen was 156 mm. of mercury or more surgical anæsthesia could not be obtained, regardless of the partial pressures of the nitrous oxide. If, however, the oxygen percentage was decreased until the partial pressure was about 70 mm. of mercury or less, apparently the animals became anæsthetized. They came to the conclusion that anæsthesia cannot be produced with nitrous oxide unless it is accompanied by some anoxæmia. These findings led them to believe that Paul Bert did not produce full surgical anæsthesia with the mixtures he used and that full surgical anæsthesia is impossible in the presence of such amounts of oxygen as are sufficient to obviate anoxæmia. They also state that with 85:15 mixtures they could not obtain analgesia, pin pricks being distinctly recognized as such, in spite of some mental confusion. These latter observations were made on human beings, presumably.

It will be seen from the foregoing that it has been proved quite satisfactorily that in laboratory animals surgical anæsthesia cannot be produced without a marked reduction in the oxygen content of the arterial blood; the results of Bert are an exception. A search through the literature on the subject, however, does not reveal any similar work done on human subjects. It is quite conceivable that, since the reaction of the nervous system of animals is less sensitive to anæsthetics than is that of man, human beings might be better subjects for nitrous oxide anæsthesia than are laboratory animals. We undertook, therefore, to find out whether anæsthesia sufficient for minor surgical operations in man could be obtained with an 80:20 mixture of nitrous oxide and oxygen and, were this possible, to discover whether cyanosis is an essential factor in its production. Incidentally, we have also determined the N_2O content of the blood during anæsthesia. Before presenting our results a few words concerning the criteria of anæsthesia and cyanosis seem pertinent.

As Greene and his associates point out, more exact definition of the signs and degree of anæsthesia is badly needed. They themselves used as a criterion respiratory movements of even rhythm and amplitude. Brown, Lucas and Henderson used the response elicited by electrical stimuli applied to the hind legs of laboratory animals. They admit that the method is open to criticism, but no other means could be devised under the circumstances of their experiments. Paul Bert exposed the saphenous nerve in animals and observed the response to its stimulation. In the observations to be recorded in this communication we have taken as criteria of anæsthesia regular, machine-like breathing, purposeless movements of the eyeballs, and the absence of memory of painful stimuli.

Lundsgaard and Van Slyke[12] define the term "cyanosis" as a diffuse bluish discoloration of the skin and mucous membranes, more marked in certain regions of the body than in others (lips, fingers, etc.), but generalized in its distribution and varying both in shade of colour and in degree of intensity in different cases, and due usually to an increase of reduced hæmoglobin. The concentration of this substance is expressed indirectly as "oxygen unsaturation", a term introduced by Lundsgaard in 1919. According to Lundsgaard, since 1 c.c. of oxygen combines with 0.75 grams of hæmoglobin, 5 grams of the latter are equivalent to 6.7 volumes per cent of oxygen unsaturation. This degree of oxygen unsaturation is regarded as the "threshold value" at which cyanosis may be expected to appear. While a number of factors influence the oxygen unsaturation in the blood stream, in ordinary nitrous oxide anæsthesia in normal subjects cyanosis may be regarded as due to the decreased re-oxygenation of the blood in the lungs on account of low oxygen tension.

THE METHOD AND RESULTS

The following observations were carried out on 14 surgical and dental patients. The 80:20 mixture of nitrous oxide and oxygen was administered from a machine (Foregger) consisting of a system of flowmeters which provide for the accurate measurement of the percentage of gases used, to 12 patients in the semi- or fully recumbent positions. In 3 patients, not recorded here, anæsthesia could not be induced, regardless of the higher concentrations of nitrous oxide used.

After the surgical procedure, and with the continued administration of the anæsthetic as before, 20 to 30 c.c. of blood were collected from the radial artery by means of a syringe containing a trace of potassium oxalate and liquid paraffin to avoid clotting and loss of gases from the blood. The blood was allowed to run into the syringe under its own pressure in order to make certain that the needle was in the artery and not in the vein. It was then transferred to a small bottle containing a quantity of oil, so

that all the air was displaced when the blood had been added. The gas determinations were carried out about fifteen minutes after the collection of the blood, which was the time necessary to bring the samples to the laboratory.

The original Van Slyke blood-gas apparatus was used to determine the amount of oxygen combined with hæmoglobin, the oxygen capacity, and the nitrous oxide content of the blood samples.[13] The total gas liberated after the addition of the ferricyanide reagent and subsequent alkalinization of the solution was measured. The decrease in volume when sodium pyrogallate was added gave the oxygen content from which the combined oxygen was calculated. The residual gas is nitrous oxide. It was assumed that by the time the blood sample was taken all nitrogen had been eliminated from the blood. Since nitrous oxide is not a highly insoluble gas, it is probable that enough remains in solution, even in the evacuated apparatus, to make the nitrous oxide results low. When the oxygen capacity was determined, it was soon found that all of the nitrous oxide was eliminated in the oxygenation procedure. Absorption of the oxygen by pyrogallate left no readable volume.

As shown in the accompanying Table, the patients ranged in age from 3 to 66 years, and were of both sexes. Their general physical condition ranged from poor to very good. One patient, No. 6, was in the eighth month of pregnancy. The majority of the patients had several or all of their teeth extracted; the surgical procedures in the other cases involved the opening and packing of a breast abscess; dilatation and curettage; and the incision and packing of carbuncles. The smoothness of induction and the depth of anæsthesia obtained were noted, together with its duration, before the blood samples were taken. Clinical evidence of the presence or absence of cyanosis was also recorded.

Patients Nos. 11 and 12 received 16 milligrams of morphine sulphate hypodermically, one-half hour before the induction of anæsthesia. Patients Nos. 13 and 14 received 17 to 18 per cent of oxygen instead of 20, since they could not be anæsthetized with the 80:20 mixture. All the other patients were given an 80:20 mixture of nitrous oxide and oxygen without any pre-anæsthetic medication.

TABLE

Patient	*Age*	*Physical Condition*	*Type of Operation*	*Duration of Anæsthesia*	*Anæsthesia*	*Induction*	*Cyanosis*	*Arter. Blood in Vol. Per Cent*			*Oxygen Saturation*
								N_2O	*Oxy. Comb. with Hb.*	*Oxygen Capacity*	
				min.							per cent
1	20	Good	Extraction	20	Deep	Smooth	None	18.46	19.22	20.24	94.9
2	3	Good	Extraction	15	Deep	Fair	None	16.81	13.34	18.00	74.1
3	24	Good	Carbuncle	30	Deep	Smooth	None	19.50	17.32	19.20	90.2
4	32	Fair	Extraction	20	Deep	Smooth	None	18.21	17.33	19.13	90.6
5	8	Good	Extraction	10	Fair	Smooth	None	17.05	16.48	17.08	96.5
6	26	Preg. (8)	Extraction	15	Deep	Smooth	None	18.59	14.09	17.50	80.5
7	24	Obese	Extraction	15	Deep	Smooth	None	20.56	15.16	18.39	82.4
8	10	Good	Extraction	10	Deep	Smooth	Present	18.68	8.73	17.94	48.6
9	26	Fair	Extraction	15	Deep	Sudden	None	21.74	13.20	17.28	76.4
10	9	Good	Extraction	15	Deep	Smooth	Airway blocked. Present	18.83	9.93	18.40	53.9
11	38	Poor	Diabetic carbuncle	30	Fair	Smooth	Slight	19.71	11.09	16.09	68.9
12	25	Good	Breast abscess	15	Deep	Smooth	None	22.68	12.54	17.26	72.6
13	66	Fair	Extraction	20	Good	Difficult	Present	19.19	8.54	18.33	46.7
14	29	Good	Extraction	15	Fair	Difficult	Present	16.38	12.39	17.91	69.1

Interpretation of the significance of the oxygen content of arterial blood during anæsthesia must of necessity take into consideration factors, apart from the administration of the anæsthetic, which in themselves may produce a lowering of the arterial oxygen content. Any mechanical obstruction of the respiratory passages tends to reduce the oxygen supply. This is a very important factor in dental operations involving operative procedures which cause a certain degree of respiratory obstruction. Saliva and blood in the mouth and throat interfere with the free passage of the anæsthetic mixture into the lungs

and the removal of the products of respiration outwards. The rapid, shallow breathing incidental to anæsthesia is in itself conducive to the production of anoxæmia and may result in reducing the arterial oxygen content to as low as 91.7 per cent saturation.[14] Also in those cases in which there is a low respiratory minute volume, or the circulation is sluggish, or when both these factors are present together, the oxygen content tends to be lower.[10] In the recumbent position, the respiratory function is not so efficient as in the upright, and, further, any interference with the movements of the diaphragm (restriction of the lower ribs or abdomen) operates in the same direction.

Nitrous oxide.—In the first 10 cases recorded, the nitrous oxide content was found to be fairly constant, ranging from 16.81 to 21.74 volumes per cent, with an average of 18.84. These figures are somewhat lower than those recorded by Greene and his co-workers for the dog.

Cyanosis.—As stated earlier, Lundsgaard regards a mean reduced hæmoglobin content of capillary blood of 6.5 volumes per cent as the threshold value at which cyanosis becomes apparent. By "mean reduced hæmoglobin content of capillary blood" is meant half the sum of the reduced hæmoglobin values of arterial and venous blood. Since we have determined the reduced hæmoglobin content (oxygen unsaturation) of arterial blood only, and know nothing of the corresponding values for venous blood, this criterion of cyanosis cannot be used to interpret our data. According to Barcroft and his co-workers,[15] cyanosis appears when the arterial oxygen unsaturation reaches 10 to 15 per cent of the total capacity. Binger, Hastings and Neil[16] found a similar state of affairs in pneumonia. If our data are judged by this standard, it will be seen that 4 of our cases show oxygen unsaturations of less than 10 per cent. In the remaining 10 cases, the oxygen unsaturations are greater than 15 per cent. Observation of the patients, however, showed that 3 patients (Nos. 2, 9 and 12) with oxygen unsaturations between 20 and 30 per cent also showed no "clinical" cyanosis. If, however, we adhere to the analytical criterion of cyanosis, it may be stated that in 4 of the 14 cases recorded we have had satisfactory anæsthesia with nitrous oxide without cyanosis. It is pertinent to inquire, therefore, whether the cyanosis present in the other instances had anything to do with the anæsthesia, or whether it was only the result of a decrease in the efficiency of alveolar ventilation, or was due to mechanical causes, as suggested above. Since 20 per cent of oxygen was administered continuously, and since the circulation is not believed to be affected greatly in nitrous oxide anæsthesia, aside from conceivable respiratory complications, there is no obvious explanation for the subnormal oxygen saturation of the arterial blood. It may be granted that cyanosis may make anæsthesia more easily producible, but the present work seems to indicate that cyanosis is incidental but not essential to nitrous oxide anæsthesia.

The above statements, naturally, apply only to man. As indicated at the beginning, other workers have shown that an 80:20 mixture of nitrous oxide is insufficient for anæsthesia in laboratory animals. This difference between man and other animals is quite understandable, since the central nervous system of the former is more easily affected by other anæsthetic agents too. Perhaps the difference between the behaviour of man and that of lower animals to nitrous oxide has received more emphasis because neither is very susceptible to nitrous oxide, and even in the case of man the effective nitrous oxide concentration is so high that latitude is not left in all instances for an adequate oxygenation of the blood. For some human beings the 80:20 mixture is, of course, insufficient, and higher ratios can easily cause cyanosis.

SUMMARY

The percentage of oxygen saturation of the hæmoglobin of arterial blood was determined in 14 cases of nitrous oxide anæsthesia.

The data lead to the conclusion that in man nitrous oxide anæsthesia is not necessarily accompanied by cyanosis. In less susceptible subjects, however, and in some instances probably because of obstruction and abnormalities of respiration, some degree of cyanosis is probably inevitable.

REFERENCES

1. ANDREWS, E., *J. Brit. Dent. Sci.*, 1869, p. 22.
2. BERT, P., *Comptes Rendus de l'Academie des Sciences*, 1878, **88**: 728.
3. BERT, P., *ibid.*, 1879, **89**: 132.
4. JOLYET AND BLANCHE, *Comp. rend. de. biol.*, 1873, Vol. **223**.
5. NICLOUX, M., Quantité de protoxyde d'azote dans le sang, au seuil de l'anesthésie, pendant l'anesthésie confirmée, au moment de la mort, *Comptes Rendus de la Soc. de Biol.*, 1908, **64**: 502.

6. OLIVIER, F. AND GARRET, F. C., An analysis of the gases of the blood during chloroform, ether, bichloride of methylene and nitrous oxide anæsthesia, *The Lancet*, 1893, **2:** 625.
7. KEMP, G. I., Nitrous oxide anæsthesia, *Brit. M. J.*, 1897, **2:** 1480.
8. LEAKE, C. D. AND HERTZMAN, A. B., Blood reaction in ethylene and nitrous oxide anæsthesia, *J. Am. M. Ass.*, 1924, **82:** 1162.
9. CULLEN, G. E., AUSTIN, J. H., KORNBLUM, K. AND ROBINSON, H. W., The initial acidosis in anæsthesia, *J. Biol. Chem.*, 1923, **56:** 625.
10. GREENE, C. W., CURREY, H. M., DEXHEIMER, F. E., HANNAN, E. B. AND HARLAN, D. L., The distribution of nitrous oxide and oxygen in the blood of dogs during gas anæsthesia, *Arch. Int. Med.*, 1925, **35:** 379.
11. BROWN, W. E., LUCAS, C. H. W. AND HENDERSON, V. E., The anæsthetic value of nitrous oxide under pressure, *J. Pharmacol. & Exper. Therap.*, 1927, **31:** 269.
12. LUNDSGAARD, C. AND VAN SLYKE, D. D., *Medicine*, 1923, **2:** 1.
13. HAWK, P. B. AND BERGEIM, O., Practical physiological chemistry, p. 450, 1926, P. Blakiston's Son & Co., Phila.
14. HALDANE, J. S., MEAKINS, J. C. AND PRIESTLEY, J. G., The effects of shallow breathing, *J. Physiol.*, 1918-19, **52:** 433.
15. BARCROFT, J., BINGER, C. A., BOCK, A. V., DOGGART, J. M., FORBES, H. S., HARROP, G., MEAKINS, J. C. AND REDFIELD, A. C., Observations upon the effect of high altitude on the physiological processes of the human body, carried out in the Peruvian Andes, chiefly at Cerro de Paseo. Report to the Peru High-Altitude Committee, *Phil. Trans. Roy. Soc.*, 1923, **B.211:** 351.
16. BINGER, C. A., HASTINGS, A. B. AND NEIL, J. M., Œdema associated with moderate bicarbonate administration during convalescence from pneumonia, *Arch. Int. Med.*, 1923, **31:** 145.

THE EARLY DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE UTERINE CERVIX*

BY A. B. WHYTOCK, B.A., M.R.C.S.(ENG.), F.A.C.S.,

Niagara Falls, Ont.

IX

"CANCER of the uterine cervix when treated in its incipiency is curable in nearly every case." If this statement, recently made by an eminent authority,[1] be true, it will be well to limit our discussion of this condition to a consideration of the predisposing factors in its causation, its earliest clinical features, and its early cure. By laying more stress on this stage of its development alone can we hope to speed our progress towards its eventual control.

The frequency of cancerous involvement of the cervix, like that of the breast, is well known. According to Kelly, 3.5 per cent of all cases admitted to the gynæcological clinic of the Johns Hopkins Hospital in fifteen years had uterine carcinoma. The treatment has become more hopeful, and it is significant to note that at the Symposium on Cancer at the meeting of the American College of Surgeons in St. Louis, of 8,840 cases of malignancy reported with cures for the five-year period, 1,561 were cases of carcinoma of the cervix.

Pathologically, the lesion is of the epitheliomatous type, 96 per cent of all cases belonging to the squamous epidermoid cell group. It arises chiefly from the epithelium of the vaginal portion or from the thickened epithelium of an erosion, the chief site of predilection being the external os. Rarely, it arises from the columnar lining of the canal and its glands, forming the relatively rare adenocarcinoma. The internal os acts like a barrier to limit spread to the uterine body, and the cancer cells gradually permeate the lymphatic spaces in the connective tissue to the parametrium, thence to the rectum and bladder. Its spread through the lymphatic vessels to the lymph nodes is capricious; sometimes early, sometimes late. Blood stream involvement is always late (Boyd).

By far the greatest number of malignant lesions of the cervix are found in women who have borne children, not over 3 per cent being reported in nulliparæ. This gives us a suggestion as to causation. Whatever the unknown constitutional intrinsic factor, it is agreed that the extrinsic factor in carcinogenesis is chronic irritation. Here we have it. The unhealed cervical tear of labour denudes the squamous portion of the portio vaginalis; then comes the inflammatory reaction with its irritating discharge, the associated endocervicitis or erosion. Perhaps the latter may come from infection alone. The cervix becomes more bulky and spongy. In long-standing cases it may contain numerous small cysts, or there may be some small polypi attached to the canal. Sexual intercourse and strong antiseptic douches do not improve conditions, and this cervix is of definitely carcinogenic type. As the years pass, there comes the insidious development at the margin of the lesion of the cells of cancer. In passing, it might be well to remind ourselves of the traumatic endocervicitis caused by the use of pessaries and supports or by the repeated amateur attempts at abortion. Mayo has

* Read at the fifty-third annual meeting of the Ontario Medical Association, Hamilton, June, 1933.

Other papers in the series on the early diagnosis of cancer can be found in the *Journal* as follows:—1933, **29:** 465; 1934, **30:** 46, 48, 50, 168, 171, 280, 283.

also called attention to the development of carcinoma in the stump of a uterus following subtotal hysterectomy, in which a slightly infected cervix had been left, the lymphatic drainage and blood supply having been interfered with. In a recent communication Dr. Gray Ward, of New York, has reported 19 such cases.

It is unfortunate that there are no typical symptoms of early cancer. Probably *hæmorrhage* of some type is the earliest. This may be simply a slight increase in the usual menstrual flow, or it may be a slight spotting noted after douching, intercourse, defæcation or following exercise. Perhaps there is the appearance of a slight offensive discharge where none was present before. There may be only an itching or irritation of the external genitals.

When the early case comes for examination and diagnosis we face a very difficult problem. When can we suspect invasion by malignancy? A laceration with flaring lips may worry us, or a nodule or thickening of the cervix; an ulcer or a polypus may give us pause; yet nothing typically malignant is found. At this juncture we may be helped by an ingenious clinical test devised by Schiller, of Vienna, which may prove to be of infinite value. It is specific for the absence of cancer. If time places a seal of approval upon it, we will have a very useful aid in diagnosis, and when positive it will be a great help in the selection of material for microscopic diagnosis. During the course of an extensive research into the earliest development of cancer of the cervix Schiller made some interesting observations. Detailed histological examination enabled him to identify the earliest carcinomatous changes in what he calls "the carcinomatous superficial layer." The histological characteristic of this layer is the presence of polymorphous and atypical cells with multiple nuclei and arranged in irregular order. The demarcation between the normal and the abnormal epithelium is distinct and always oblique, with the carcinomatous layer wider at the base than on the surface. Normally, the superficial cells of the cervix are filled with glycogen; this is absent in the abnormal cells. Schiller, therefore, discovered that the cervix painted with Lugol's solution would stain a mahogany brown, the glycogen-free carcinomatous layer remaining unstained. This unstained area must be suspected as potentially malignant and examined histologically. Following the test it is sufficient to scrape off a very small piece of epithelium with a spoon without incising the part. This specimen should be taken not from an ulcerated or eroded area but from the whitish superficial stripe around the ulceration, if present, and as indicated by the test. In positive cases the Lugol's stain gives a definite outline of the extent of the area to receive radical treatment. Having had one extremely interesting early case diagnosed by this method and successfully treated, may I commend it to you as worthy of careful trial.

Coming now to consider the treatment of early cases, it seems perfectly obvious where our duty lies. It behoves us to look upon all irritative lesions of the cervix as serious. Whenever it is possible the tear of the cervix during labour must be repaired. If inconvenient or difficult at the time every case must be examined subsequently for lacerations and treated accordingly. Endocervicitis should not be neglected or passed over by the prescription of a douche. It is as important as a pathological appendix, both as a focus of irritation and as a nidus for cells of potential cancer. We cannot say that we do not see these cases, nor deny that we frequently neglect them. Many cases of carcinoma which we see have been treated superficially by other physicians. Our policy of *laissez faire* must be changed. The indications for treatment of endocervicitis are satisfactory. Generally speaking, if the cervix is painted with simple tincture of iodine and it takes the stain it will usually respond to medical treatment. If it does not retain the stain cautery, radium, or operation will be indicated. Although the treatment of endocervicitis is not within the scope of this discussion it might be well to refer to the value of such topical applications as silver nitrate, 4 to 10 per cent, potassium permanganate powder applied to the eroded area at weekly intervals, mercurochrome, 20 per cent. It might be well to refer to the importance in the acute case of rest in bed and hot douches, taken not in the crouching but in the recumbent position, with the hips elevated, using weak permanganate solution, hypertonic saline with sodium bicarbonate, or, for a longer period, pure lactic acid, one drachm to a quart of water.

In severe and resistant cases we must have

recourse either to cautery or operation. As regards the former no reference would be complete without mention of the excellent results reported everywhere by diathermy, using the bi-polar method, the technique of which may be carried out as an office procedure. As regards surgery, certain cases do well with a simple trachelorrhophy or a Schroeder or Sturmdorf operation. Whatever the method, we must be more radical in the treatment of these lesions. Finally, what of the early carcinoma? Are we to advise surgery or radium? Each still has its advocates. We have the cautery operations, *e.g.*, high amputation, as advocated by Byrne, or the slower method of Percy. In surgery, we have the total hysterectomy of Wertheim, still advocated by such master surgeons as Bonney. However, if we can interpret present-day statistics aright, the future lies with radium, and we have such authorities as Döderlein, of Munich, declaring that for carcinoma of the cervix the day of surgery is over. Fortunately, experience has shown that 20 per cent of all cases of carcinoma of the cervix are in the radio-sensitive group, and the earlier the lesion the more radio-sensitive. There is no immediate mortality from the treatment, and there are more competent radio-therapeutists than there are surgeons qualified to do a Wertheim hysterectomy. The statistics from all the large clinics where radium is used are improving year by year, and in the early case particularly it is quite dramatic to witness the wonderful result which the application of the proper dose of radium has upon the lesion. Let us have no hesitation whatever after an early diagnosis has been made or suspected in turning the case over to the radio-therapeutist for active treatment.

In conclusion, we must recognize that the responsibility for the success of our campaign to control this disease rests with every general practitioner. He must be careful of the little things in cervical pathology lest the big lesions follow. His success will be incomplete unless he plays his part in educating the public. He can foster the popular interest in cancer, decrease the ignorant fear and superstition concerning it, and impress upon all women the importance of keeping the cervix clean, healthy and free from disease. Schiller would have us examine every woman twice or three times a year by his Lugol's test. This might be difficult, but a far larger percentage of our female population might be induced to follow the school of thought recently championed by our large insurance companies, and every woman might well be urged to have a pelvic examination on her birthday.

REFERENCES

1. BURHAM, *Surg., Gyn. & Obst.*, 1933, **56**: 427.
2. SCHILLER, *Ibid.*, 1933, **56**: 210.

CONCOMITANT SQUINT

BY W. H. MONTAGUE THOMSON, M.D.,

London, Ont.

CONCOMITANT squints are quite common, and as they practically all can be corrected it is unfortunate that so many are totally neglected or improperly treated. Squint is defined as a deviation of one of the eyes from its proper direction so that the visual axes cannot both be directed simultaneously at the same objective point. When the squinting eye is powerless to follow the movement of its fellow in one or more directions the condition is said to be *paralytic* and is usually the result of tertiary lues, severe debilitating infections, or increased intracranial pressure. When the squinting eye follows the movement of its fellow to some degree, in all directions, the condition is known as *concomitant squint* and it is to this type of squint that attention is drawn in this article.

The "cross-eyed" child is so often the object of thoughtless remarks that the whole personality may be altered, and later in life the defect is a serious handicap in any profession. The cosmetic imperfection is alone a good reason for correction, but there is a functional one as well. When one eye turns in or out the ability to judge depth and distance suffers through lack of binocular vision.

It is customary to classify concomitant squint according to the direction of deviation, *viz.*: (1) esotropia—the eye turns inwards (cross-eye); (2) exotropia—the eye turns outwards;

(3) alternating—(convergent or divergent)—either eye is able to fix, its fellow meanwhile deviating; (4) sursumvergent—the eye turns upwards; (5) deorsumvergent — the eye turns downwards. Sursumvergent and deorsumvergent squint are rarely seen, and unless they are of marked degree operative procedures should not be attempted, as these are generally unsatisfactory.

In attempting to explain concomitant squint four main factors have been advanced, namely: anomalous muscle insertion, amblyopia of an eye preventing fixation, poor development of fusion power, and refractive errors. One or all of the foregoing factors may be inherited.

There can be no question that uncorrected refractive errors in children are often responsible for squints.[1] Normally, accommodation and convergence are very intimately linked together, so that when the eyes accommodate to observe a near object the refractive power of the lenses increases and the eyes simultaneously converge to a degree proportionate to the amount of accommodation. When an uncorrected hyperopic (far-sighted) person observes a near object he must accommodate as much more than a normal person as he has diopters of hyperopia. This excessive accommodative effort tends to cause the patient's eyes to converge excessively because of the direct ratio between accommodation and convergence. If there is too much convergence the visual axes will meet too close to the eyes, so that eventually, to see near objects distinctly and without undue muscular strain, the patient either partly dissociates accommodation and convergence or lets one eye turn inwards, allowing the other eye to focus the object alone. Conversely, an uncorrected myopic or short-sighted person is liable to develop an exotropia (divergent squint) because here convergence is used in excess of accommodation. It follows that it is imperative to correct refractive errors in children who have squints at an early age so that the balance between accommodation and convergence as well as binocular vision will not become greatly impaired.

Esotropia usually appears soon after the child becomes interested in near objects and such children in 90 per cent of cases are hyperopic. Exotropia generally appears later than esotropia and the persons concerned are quite frequently myopic.

A child two years of age or less is too young to wear glasses, but the good eye can be temporarily fogged either by a bandage which may be removed at night or by instilling 1 per cent homatropine solution twice daily on alternate days. Either method may be safely continued under supervision for 3 to 4 months and serves to compel the child to use the squinting eye whose image would otherwise be suppressed. From about 2½ or 3 years of age most children can be taught to tolerate glasses. An old frame without lenses can be adjusted by the optician and the little patient forced to wear this for 3 to 4 weeks. This will save the proper lenses from being broken when they are fitted. By the early and correct use of glasses a large number of squints will be cured. If, however, after six months the squint remains, some type of muscle operation is necessary and should be done. The parents should be advised that more than one operation may be necessary to straighten the eyes. From 4 to 10 years of age is an ideal time to operate, from 10 to 20 years is generally satisfactory, from 20 to 30 years the eyes can be straightened, but one is not so sure they will remain straight. After 30 it is doubtful if any operation should be advised, for the correction is frequently not permanent. Some do not advise operation before 8 years; however, the earlier the operation is performed the better the prospect of binocular vision. Up to 15 years and for all tucking operations a general anæsthetic is to be preferred. It is true the anæsthetic often temporarily abolishes the convergent squint, or transfers it to the good eye, and under such conditions the correction cannot be estimated so surely as under cocaine, but the ease of procedure under general anæsthesia makes up for these deficiencies.

Alternating divergent squint is very rare; alternating convergent squint is more common. While both types can be corrected for a cosmetic result I have never seen binocular vision obtained and frequently the full correction is not permanent.

The general consensus as far as surgical procedures are concerned is that the same result may be obtained by a variety of operations. The following methods are mentioned only because of familiarity with them; in no sense are they considered to be the only methods of value.

A recession of the internal rectus muscle at-

tachment of the squinting eye is an effective and relatively simple method to correct esotropia of less than 30 degrees. Reese[2] of Philadelphia after completely freeing the internal rectus for a length of about ½ in., severs the muscle close to the sclera in front of a Worth clamp. One needle of a double arm silk suture is then made to pick up about 3 mm. of the outer scleral fibres and continued through the muscle in front of the clamp. The other arm of the suture is likewise placed through the muscle in front of the clamp and both needles removed. The muscle is now tied to its new attachment as the assistant slowly releases the clamp. Care should be taken to test the suture beforehand, for if it breaks the muscle retracts from sight and is not easily found. Immediate overcorrection must be aimed at and a 5 to 6 mm. recession is usually necessary, but the new attachment should never be placed behind the equator or poor rotating power may result. If the squinting eye has 6/30 vision or less, or if the patient is past 20 years of age, it is a good plan to overcorrect at operation less than one would ordinarily for fear of a permanent overcorrection. The conjunctival wound is closed with a couple of fine silk sutures, 1 per cent atropine solution instilled in both eyes, 1-3000 bichloride ointment smeared on the lid margins, and the eyes bandaged. With children it is essential to cover the eyes very securely as they often try to "peek", and if convergence is used before the muscle has securely reattached the result is much impaired.

O'Brien,[3] in doing a recession operation, uses a single-arm suture of 20 day No. 00 catgut. The conjunctiva is incised and the muscle well freed as in the preceding operation. The needle is passed through conjunctiva, muscle and sclera, then out through muscle and conjunctiva and the suture is tied over the conjunctiva. A point to be remembered here is to start far enough back in the conjunctiva so that when the suture is finally tied there is sufficient loose conjunctiva to adequately close the wound. When the esotropia is over 30 degrees either a bilateral recession or an advancement together with a recession is usually necessary. An advancement corrects about one-half as much esotropia as a recession of the same amount, and it is best in squints of over 25 degrees to do a recession and an advancement later if necessary.

The Worth operation[4] is a good one, although the two sutures are a little complicated at first, but it has the advantage of fanning the muscle out over the sclera. Proper care is necessary or the needles may be inserted too deeply and injury to the ciliary body result. It is also important in all recession and advancement operations to make sure that the new attachment is placed directly on the horizontal meridian and not above or below it or a vertical deviation may result. Jameson[5] has devised a needle which has the eye on the side and this greatly facilitates pulling the suture through the sclera; it makes any recession or advancement much easier and safer. The tucking operation eliminates the danger of needle puncture and improper placement. Parker[6] does muscle tucks regularly on exotropias and esotropias, and in conjunction with the tuck he does a guarded tenotomy of the opposing muscle. In cases of exotropia, which are always more than ordinarily hard to correct this operation is singularly useful. There is more local reaction than after a reattachment operation and a small nodule is left due to the tucked-up bit of muscle, but this disappears in 6 to 8 weeks and I have never seen a muscle tuck slough.

It is doubtful if a complete tenotomy is ever justified. If correction is not obtained after a complete tenotomy, the surgeon never knows where the muscle may be picked up when a second operation is done, and the ocular rotation is frequently not full in the direction in which the tenotomized muscle turns the eye. In exotropias no mydriatic should be used after operation and the treated eye should be covered for only a day or two in order that convergence may be trained as early as possible.

The better the visual acuity in the squinting eye, the more the squint should be overcorrected at the time of operation. After operation for esotropia the eye should be uncovered a couple of minutes daily and atropine instilled. Sometimes the overcorrection has been so great that it is wise to uncover both eyes at the end of 5 or 6 days, especially if the visual acuity of the squinting eye is poor, but usually they should be covered for 13 to 14 days.

It is true that the great majority of squints operated upon after 10 years of age never obtain binocular vision, and yet the eyes remain straight. Nevertheless it is the ideal and should be aimed at, once cosmetic perfection has been obtained by operation. In children, fusion

training offers a good hope of restoring binocular vision and should be begun 2 to 3 weeks following operation, using an amblyoscope or some similar device.

SUMMARY

1. Practically all concomitant squints can be straightened by:— (*a*) temporary covering or fogging the good eye in children; (*b*) the early use of properly fitted glasses; (*c*) failing these methods, operative procedure is indicated; (1) recession for squints of high degree; (2) advancement for squints of low degree, or to be used together with a recession for high degree squints; (3) tucking with a guarded tenotomy.

2. Following correction for a cosmetic result, fusion training should be used.

REFERENCES

1. BALL, J. M., Modern Ophthalmology, Davis, Phila., 1916, p. 679.
2. REESE, W. S., personal communication.
3. O'BRIEN, T. A., personal communication.
4. GRIMSDALE, H. B. AND BREWERTON, E., A Text-book of Ophthalmic Operations, Macmillan, Toronto, 2nd ed., 1920, p. 31.
5. JAMESON, P. C., *Arch. Ophth.*, 1931, **6**: 329.
6. PARKER, F. C., *Arch. Ophth.*, 1932, **8**: 727.

LA POLIOMYELITE DANS LA VILLE DE QUEBEC EN 1932

PAR EDGAR COUILLARD, B.A., M.D., D.P.H.,

Professeur d'Hygiène à l'Université Laval; Inspecteur Régional pour le Service Provincial d'Hygiène de la Province de Québec; Membre de l'American Public Health Association, Québec

LA ville de Québec étant comprise dans le territoire d'inspection régionale qui nous est dévolu, nous avons eu l'avantage non seulement de suivre de près la marche de la poliomyélite, mais aussi de pouvoir observer un très grand nombre de malades. L'année 1932 restera à bon droit célèbre, dans les annales médicales de la ville, par l'épidémie considérable dont cette maladie a été la cause. C'est l'histoire de cette épidémie, son évolution et les quelques enseignements qu'elle comporte que nous nous proposons de fixer ici.

La présente étude comprend toute l'année 1932, et non pas seulement la période de l'épidémie; les quelques mois de recul ajoutés avant et après l'épidémie, nous ferons mieux voir les périodes de l'envahissement et du déclin de l'infection; et les quelques rares cas (cinq en tout) survenus durant l'année, mais en dehors de la durée réelle de l'épidémie, ne modifient que très peu, dans un sens ou dans l'autre, les chiffres obtenus au cours de notre compilation.

Historique et distribution chronologique.— L'épidémie due à la poliomyélite en 1932 a eu un prélude parmi la population même de la ville, comme en font foi les données suivantes que nous avons pu recueillir au cours de nos investigations. D'abord, en août, 1928, un cas; l'enfant atteint, que nous avons vu en novembre dernier (1932), a conservé une lésion paralytique dans son membre inférieur gauche. En 1929, quatre cas nous sont signalés durant la deuxième semaine du mois d'août, et un cinquième cas le 6 septembre. C'est aussi en 1929, et au même moment (août et septembre), que des cas de la même affection nous furent signalés par les médecins des hôpitaux situés dans la ville, chez des enfants malades venus de la Malbaie (Cté de Charlevoix), du Lac-Saint-Joseph, et de Ste-Catherine (Cté de Portneuf), de St-Gérard-Magella et de Sillery (Cté de Québec), de Bienville (Cté de Lévis), et de la ville de Montmagny. Si, dans tous ces endroits, les manifestations de la poliomyélite ne dépassèrent pas l'état sporadique, déjà à ce moment il était permis d'entrevoir que la maladie, prenant pied plus fermement dans notre région, encerclant un peu plus étroitement le territoire de la ville, devait modifier, peut-être bientôt, la constitution médicale de sa population. Notons aussi, en passant, à cause de l'intérêt historique que ce fait comporte, que c'est en 1929 que le sérum de convalescent antiparalytique fut employé pour la première fois, sauf erreur, à Québec.

En 1930, nous n'avons relevé qu'un cas survenu le 2 avril; l'enfant fut lésé dans ses deux membres inférieurs.

L'année 1931 fut plus remarquable, et c'est ici que se trouve le prélude qui annonce ce que sera 1932: d'abord, le 27 janvier, 1 cas; puis aucun,

jusqu'à la troisième semaine du mois d'août exclusivement. Les 3e et 4e semaines d'août et la 1ére semaine de septembre, 2 cas chacune; la 2e semaine de septembre, rien; la 3e et la 4e semaines, 2 cas; le 1ère semaine d'octobre, 3 cas; puis 3 autres cas durant le 3e semaine; 1 cas durant la première semaine de novembre; et enfin, le dernier cas de l'année la 3e semaine du même mois. Nous avons donc, en 1931, un total de 19 cas de poliomyélite, qui ont tous pris leur origine dans la ville et chez des personnes qui y demeuraient.

Nous voici en 1932. Le premier cas survient le 17 mars; un autre le 20 juin, et un troisième cas le 2 juillet. Donc, durant les six premiers mois de 1932, la maladie continue à évoluer à l'état sporadique tout comme durant les deux derniers mois de 1931, et reste telle jusqu'à la troisième semaine de juillet, alors que la situation se complique et que la maladie marche rapidement vers l'épidémicité.

Le graphique No 1 nous donne une vue d'ensemble du nombre des cas par semaines, et nous permet de faire la comparaison avec l'année 1931. Nous y voyons que l'épidémie commence réellement durant la troisième semaine de juillet, c'est-à-dire un mois plus tôt que la petite éclosion précédente de 1931, alors que les cas sporadiques se firent plus nombreux à partir de la troisième semaine du mois d'août seulement. La troisième semaine de juillet nous notons 3 cas; la semaine suivante, 1 cas seulement; puis, 6; puis, 7 cas la 4e semaine depuis le début de l'épidémie. Mais celle-ci précipite sa marche, et elle atteint sa période d'acmé dès la septième semaine (la dernière du mois d'août), qui fournit un contingent de 37 malades. Puis, dès le début de septembre, léger déclin qui reste stationnaire durant tout le mois (24, 26, 25 et 28 cas par semaine, respectivement). En octobre, déclin la première semaine (20 cas), encore plus accentué la semaine suivante (13 cas). Puis, l'épidémie durera encore quatre semaines consécutives avant de s'éteindre avec la première semaine de novembre (5 cas). Enfin, le 14 novembre 1 cas; puis le dernier et le deux cent quarante-huitième cas de l'année survient le 10 décembre. L'épidémie est bien terminée; sa durée a été de dix-sept semaines.

Distribution topographique.—Pour celui qui connaît le territoire de la ville de Québec, il est facile de se rendre compte que son territoire peut être divisé en deux parties nettement distinctes l'une de l'autre géographiquement par la différence de leur niveau: la partie basse qui entoure le promontoire, située au niveau de la mer, et la partie haute qui couronne son sommet. Or, la poliomyélite réapparaît en 1932, d'une manière décisive, dans la partie basse; les 38 premiers cas y sont tous localisés depuis le début jusqu'au 15 août, par conséquent jusqu'à la sixième semaine de l'épidémie; elle y a déjà fait 5 victimes. De même, la maladie disparaîtra, mais moins nettement, par la partie basse où seront localisés les 3 derniers cas de la dix-septième semaine, et aussi 2 cas ultérieurs, soit les 5 derniers de l'année. En réapparaissant cette année dans la partie basse du territoire, où elle s'était maintenue presque exclusivement (18 cas sur 19) l'année précédente, la poliomyélite ne faisait que raviver les foyers d'infection déjà établis.

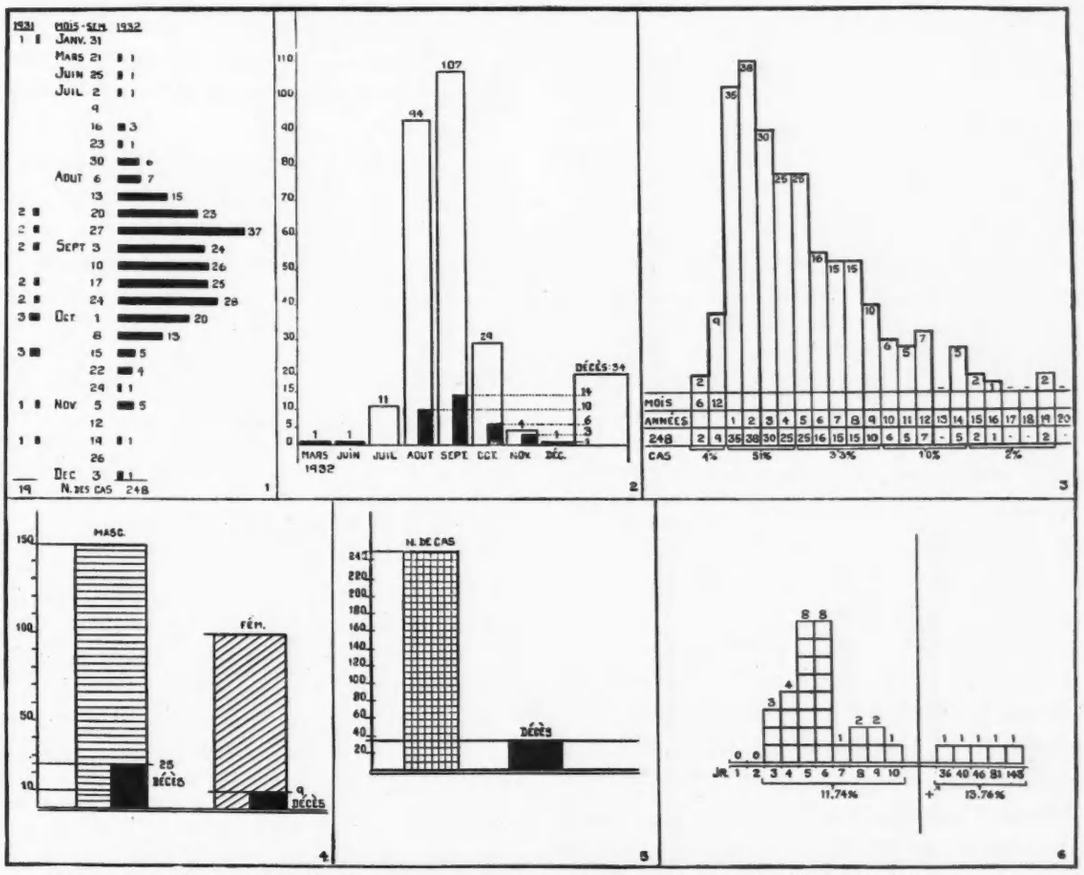
Puis elle accède dans la partie haute avec le trente-neuvième cas, qui meurt 5 jours plus tard (c'est le sixième décès depuis le début). Nous sommes à la sixiéme semaine, et nous avons vu précédemment qu'au point de vue du nombre des cas, l'épidémie est près de son maximum (septième semaine). Nul doute que la virulence de l'infection est aussi à son maximum d'intensité lorsqu'elle atteint la partie haute du territoire.

Outre ce qui prédède, je résume les observations au point de vue topographique:—1° la partie haute a 83 cas, et une mortalité de 15.7 pour cent; la partie basse a 165 cas, et une mortalité de 12.7 pour cent;—2° la répartition des cas par rues, est la suivante: 71 rues ont un cas seulement;—38 rues en ont 2;—17 en ont 3;—6 en ont 4;—6 en ont 5;—3 en ont 6;—et 2 rues en ont 8;—soit un total de 248 cas distribués dans 134 rues;—3° les cas sont répartis indifféremment dans l'espace, ici et là, comme au hasard, et sans aucun lien les uns avec les autres, semble-t-il, isolés les uns des autres, et séparés le plus souvent par de grandes distances. La maladie a recouvert à peu près également tout le territoire de la ville, jusqu'à ses extrêmes limites ouest et nord-ouest (av. Holland,—1148, chemin Ste-Foy,—395, rue de la Canardière) sans créer aucun foyer prédominant. Les classes riches ont été tout aussi atteintes que les classes pauvres. La maladie n'a pas sévi davantage dans les quartiers populeux; tous les quartiers ont été visités.

Total des cas.—Durant l'année 1932 il y a

eu parmi la population de la ville 248 cas de poliomyélite reconnue, dont le diagnostic n'admet aucun doute. Deux cent trente-six cas ont pris leur origine dans la ville même, et 12 dans d'autres localités où ils étaient en villégiature, mais tous sont revenus à la ville, dès le début, faire leur maladie et y être traités par leur médecin de famille.

indique le nombre des cas et celui des décès pour chaque mois concerné. Quatre-vingt-un pour cent des cas sont survenus en août (94) et septembre (107), ainsi que 70 pour cent des décès. Un malade atteint de la poliomyélite le 12 août, est décédé le 1er janvier 1933. L'état épidémique est bien classiquement situé "à la fin de l'été au début de l'automne", avec pré-



GRAPHIQUE No 1.—Distribution par semaine et comparison des années 1931 et 1932.
GRAPHIQUE No 2.—Distribution et mortalité mensuelles.
GRAPHIQUE No 3.—Distribution selon l'âge.
GRAPHIQUE No 4.—Distribution et mortalité par sexe:—Sexe M.: 150 cas, 60.88 pour cent; mortalité, 16.6 pour cent.—Sexe F.: 98 cas, 39.12 pour cent. Mortalité, 9.18 pour cent.
GRAPHIQUE No 5.—Mortalité globale. N. de cas, 248. Décès, 34. Mortalité, 13.7 pour cent.
GRAPHIQUE No 6.—Jour du décès après le début de l'infection.

Il n'y a aucun doute que les formes frustes et abortives de la même infection ont été fort nombreuses, car au cours de l'épidémie des accès fébriles simples, des troubles gastro-intestinaux et aussi pulmonaires, mais de courte durée et sans suite, ont été observés en grand nombre chez des enfants de tout âge.

La morbidité générale a été de 175 par 100,000 habitants: taux assez élevé qui témoigne de l'intensité de l'épidémie, et qui est, à peu de chose près, le double de celui de l'épidémie de poliomyélite de Montréal, en 1931 (environ 89).

Distribution mensuelle.—Le graphique No 2 dominance trèsnette durant les mois d'août et septembre.

Distribution par sexe.—Le graphique No. 4 donne, pour chaque sexe, le nombre des cas, celui des décès et la mortalité. Soixante et un pour cent appartiennent au sexe masculin, et 39 pour cent au sexe féminin. La prédominance du sexe masculin est un fait normal au course des épidémies de poliomyélite, mais ici, elle nous parait quelque peu exagérée surtout en ce qui concerne la mortalité (25 décès masculins contre 9 féminins).

Distribution selon l'âge.—Le graphique No. 3

montre la répartition des cas selon l'âge respectif des malades, depuis moins de 6 mois, de 6 et 12 mois, puis de 1 jusqu'à 20 ans. Les deux plus jeunes malades étaient âgés respectivement de 3 et 6 mois, et du sexe masculin; les deux plus vieux avaient 19 ans, et étaient du sexe féminin. Tous les âges sont représentés depuis 3 et 6 mois, jusqu'à 19 ans, excepté 13, 17 et 18 ans. Nous obtenons les groupes d'âge suivants:

Groupes d'âge	*Pourcentage*
0 à 1 an	4
1 et 4 ans	51
5 et 9 ans	33
10 et 14 ans	10
15 et 19 ans	2

Plus de la moitié des cas, soit 55 pour cent, sont survenus chez des sujets âgés de moins de cinq ans, avec prédominance très nette chez ceux âgés de 1, 2 et 3 ans, ce qui est conforme à la moyenne généralement observée en France (Bertin-Sans), et en Belgique (L. Laruelle, Bruxelles 1929-1932), et aussi conforme à la norme admise aujourd'hui. Un seul et unique cas âgé de 24 ans nous a été signalé; nous l'avons éliminé parce que le diagnostic en était fort douteux, et d'ailleurs il ne modifierait pas les données numériques qui précèdent.

Contagion.—(a) Origine apparente: Douze malades semblent avoir contracté l'infection au cours de leur villégiature à la campagne, soit cinq pour cent; et 236 l'ont contractée dans la ville même d'où ils n'étaient pas sortis, soit 95 pour cent. Nous avons conservé ces douze cas avec ceux de la ville: 1° parce qu'ils font partie de la population de la ville, qu'ils y habitent et qu'ils y sont rentrés dès le début de leur maladie; 2° parce que les autres membres de ces familles avaient des relations quotidiennes avec la population active de la ville, où ils venaient traiter de leurs affaires. Il est tout aussi probable que l'infection leur ait été apportée par des porteurs de germes adultes fréquentant la ville où sévissait l'épidémie, qu'il est probable qu'ils l'aient contractée localement.

(b) Distribution dans les familles, et nombre des enfants dans chacune: Deux cent seize familles ont été visitées par la poliomyélite. Sur ce total, voici quels sont les cas simples et multiples:

N. de Cas	*N. de Familles*	*N. des Enfants dans les Familles*
Trois	1 de	3
"	1 "	7
	1 "	10
Deux	3 de	2
"	3 "	3
"	3 "	4
"	2 "	5
"	5 "	6
"	3 "	7
"	1 "	8
	1 "	9
Un	16 de	1
"	45 "	2
"	21 "	3
"	29 "	4
"	17 "	5
"	18 "	6
"	15 "	7
"	12 "	8
"	7 "	9
"	5 "	10
"	3 "	11
	2 "	12

Deux institutions de bienfaisance (hospices), abritant plusieurs centaines d'enfants, n'ont eu que deux cas chacune. Un hôpital (section des enfants) a eu un cas chez un opéré récent.

La contagion directe ou familiale semble avoir été absolument nulle ou négligeable au cours de cette épidémie:—Cas simples, 77 pour cent; cas doubles, 19 pour cent; cas triples, 4 pour cent seulement.

(c) Contacts:—La contagion directe d'une enfant à une autre n'apparaît pas davantage: chez 193 malades nous n'avons relevé aucun contact connu. Douze malades avaient été en contact avec des cas antérieurement connus soit dans la même famille, soit entre voisins, soit en jouant avec d'autres enfants dans la rue. Cinq malades appartenaient à trois groupements collectifs différents, abritant chacun quelques centaines d'enfants.

Sur 107 cas de poliomyélite survenus depuis l'ouverture des classes jusqu'à la fin de l'année, 31 malades seulement fréquentaient 22 groupes scolaires différents: cas simples dans 15 écoles; cas doubles dans 5, et cas triples dans 2 écoles. Si nous ajoutons que douze fois seulement des frères ou des sœurs fréquentaient un milieu scolaire, je crois qu'il n'est pas exagéré de dire que ce milieu est demeuré insensible à la contagion, les données précédentes établissant qu'il n'y a eu aucun foyer scolaire de l'infection poliomyélitique. Quatre autres malades avaient fréquenté un terrain de jeux durant la vacance;

un autre avait visité, une ou deux fois, une plage à proximité de la ville. Aucun groupe de malades n'a pu être rattaché à un fournisseur quelconque de denrées alimentaires. Il résulte de ce qui précède que le mode de contagion est en dehors des données positives que nous avons pu recueillir.

Sur un total de 248, dix malades avaient été vaccinés contre la diphtérie par l'anatoxine de Ramon; deux autres ont fait la poliomyélite au cours de la vaccine: un, au quatrième jour, l'autre au 10 ou 12e jour après la vaccination antivariolique.

Certains auteurs mentionnent l'influence des maladies infectieuses antérieures dont la convalescence favoriserait l'éclosion de l'infection poliomyélitique. Les faits que nous avons relevés sont plutôt rares, et partant négatifs. Un malade a été atteint au cours de la coqueluche; un autre était convalescent de la varicelle; un troisième, alors qu'il était à peine convalescent d'une diphtérie grave. Ce dernier malade commence une diphtérie le 26 octobre; le 1er novembre il va mieux et semble hors de danger; le 8, il est paralysé, faisant une paralysie du type ascendant, à évolution rapide; il est en période aiguë d'une poliomyélite grave, et meurt le lendemain. Tous les autres malades étaient apparemment bien portants lors du début de leur poliomyélite.

Mortalité.—Trente-trois malades sont décédés durant l'année 1932, et un le premier janvier 1933: le taux de mortalité est donc de 13.7 pour cent (graphique No. 5).

C'est le taux moyen normal actuellement observé. La province de l'Alberta, en 1930, a eu un taux de mortalité de 20 pour cent, sur un ensemble de 150 cas, taux considéré comme étant très élevé (cf. *Can. Pub. Health J.*, déc. 1931). D'après Pasteur-Valery-Radot, (cf. *Revue des Deux Mondes*, 15 déc. 1930), la mortalité varie avec les épidémies de 6 à 30 pour cent; depuis les quelques dernières années, ajoute-t-il, la mortalité générale moyenne est de 10, 12 et même 15 pour cent. Ce taux de 13.7 pour cent représente la mortalité globale, comprenant tous les décès survenus. Mais si nous tenons compte du jour du décès par rapport à celui du début de l'infection chez chaque malade, (graphique No. 6) nous constatons que 29 décès sont survenus du troisième au dixième jour, c'est-à-dire durant la phase aiguë de l'infection, la poliomyélite étant seule en cause; et 5 décès, du 36e au 143e jour, à la suite d'autres affections, la poliomyélite n'intervenant alors que comme cause éloignée. Nous obtenons ce qui suit:

Mortalité	immédiate	11.7 pour cent
"	éloignée	2.0 " "
"	globale	13.7 " "

Je crois que le taux de 11.7 pour cent est plus précis en autant que l'épidémie elle-même est concernée.

D'après Wickman, "c'est entre le troisième et le septième jour que la mort survient de préférence": notre graphique No 6 confirme cette assertion.

La répartition de tous les décès selon l'âge des sujets atteints nous fait voir que 73 pour cent des décès sont survenus de 0 à 5 ans, groupe d'âge qui a aussi donné la majorité des cas (55 pour cent); après 5 ans, la mortalité est devenue plus rare, et il n'y a eu aucun décès après l'âge de douze ans. Par conséquent, parmi la population de la ville de Québec, en 1932, la mortalité n'a pas augmenté avec l'âge des sujets atteints, contrairement à ce qu'affirme Dopter (cf. *Nouveau Tr. de Méd.*, Fasc. IV, p. 17), et contrairement à ce qui a été observé lors de plusieurs épidémies de poliomyélite.

Chez les garçons, la mortalité a été de 16.66 pour cent; chez les filles, de 9.18 pour cent. Il y a là une différence notable.

POLIOMYÉLITE ET SÉRUM DE CONVALESCENT

1° *Résultats obtenus.*—Ayant eu à contrôler personnellement le diagnostic de l'affection en cause, en vue de l'opportunité ou non d'administrer le sérum, nous avons pu, directement, par nous-même, dans la majorité des cas, indirectement, pour les cas que l'urgence ne nous permettait pas de visiter immédiatement, par des informations obtenues des médecins et des familles, et en utilisant les notes prises sur nos fiches pour chaque cas au fur et à mesure de leur développement, nous avons pu, après avoir contrôlé les faits, établir la compilation suivante des résultats obtenus. Le cadre que nous nous sommes tracé en établissant cette compilation sans idée préconçue, ne comporte que des faits facilement constatables, et pour cette raison, croyons-nous, demeure dans les limites positives qui n'admettent que peu ou pas d'erreur. Nous avons pris le soin de revoir les sujets atteints, plusieurs mois après leur maladie, dans le but de confirmer ou d'infirmer les résultats obtenus antérieurement, c.-à-d. immédiatement à la fin de la phase aiguë de l'infection.

L'expression *guérison*, telle qu'employée ici, s'applique exclusivement à la phase aiguë de la

maladie, dont la durée moyenne a été de trois à quatre semaines. Parmi les décès, nous n'incluons que les malades décédés au cours de cette même phase aiguë, excluant par conséquent les 5 décès survenus du 36e au 143e jour après le début de l'infection, et qui ont été immédiatement causés par des affections pulmonaires.

POLIOMYÉLITE: TOUS LES CAS, 248
A—Ont reçu le sérum de convalescent.....219
1°—A la période *pré-paralytique*.....110
Guérison sans paralysie..91 (82.72%)
Guérison avec paralysie..11 (10%)
Décédés 8
Mortalité, 7 pour cent.
2°—A la période de *paralysie*.....109
Guérison sans paralysie..13 (11.11%)
Guérison avec paralysie..78 (72.22%)
Décédés 18
Mortalité, 16 pour cent.
B—N'ont *pas reçu* le sérum de convalescent.....28
Guérison sans paralysie.. 3 (10.70%)
Guérison avec paralysie..22 (78.57%)
Décédés 3 (10.70%)
C—Sang total (paternel) avant paralysie (Guér. s. p.) 1

Les chiffres précités ont-ils une valeur absolue? Il faudrait méconnaître tous les inconnus que comporte l'évolution clinique de la poliomyélite à sa phase aiguë, pour oser le prétendre. Mais, tout en n'accordant à ces chiffres qu'une valeur relative, on peut tenir pour certain qu'un nombre important de malades, sinon tous, ont vu leur situation s'améliorer, grâce au sérum, lequel a pu intervenir soit en empêchant totalement l'apparition de la paralysie, soit en réduisant au minimum les troubles paralytiques, soit en diminuant la gravité des paralysies, soit enfin en augmentant leur curabilité ultérieure. Il est impossible, nous le savons, d'apporter des preuves irrécusables de ces faits, mais nous avons la ferme conviction que le sérum de convalescent, tel que préparé selon la technique classique et avec le soin que le sérologiste du laboratoire du Service Provincial d'Hygiène y a apporté, a dû produire, chez les malades qui l'ont reçu à Québec en 1932 les effets signalés par ceux qui ont préconisé son emploi (Netter, en 1914), ainsi que par les nombreux cliniciens qui les ont suivis et qui utilisent le sérum, convaincus que la thérapeutique actuelle n'offre aucune arme plus efficace. En adoptant cette formule, nous ne croyons ni contredire, ni amoindrir la pensée les maîtres de la science sur ce sujet, mais au contraire nous ne faisons que suivre leurs enseignements. Mais un fait nous a tout particulièrement frappé, et nous voulons le signaler en terminant. C'est que dans les formes de la poliomyélite à infection profonde, immédiatement graves, l'injection du sérum semble n'avoir eu aucune influence sur l'évolution de l'infection, comme en font foi les décès survenus les jours suivants. Le total de ces décès n'est certainement pas très considérable, dans notre présente statistique, pour justifier une conclusion aussi absolue. Il n'en est pas moins exact que chez ces sujets observés, malgré l'injection de 25 ou 30 c.c. de sérum, la maladie a continué son évolution vers le dénounement fatal sans rémission des symptômes généraux, et les malades sont décédés en pleine phase aiguë, les jours suivants. Des 34 victimes de la poliomyélite, 3 n'avaient pas reçu le sérum. Un est décédé le troisième jour; un, le cinquième, et un autre, le sixième. Cinq sont décédés tardivement (du 36e au 143e jour) de maladies intercurrentes: 2 de broncho-pneumonie, et trois de congestion pulmonaire. Les 26 autres victimes appartenaient bien à la phase aiguë, et toutes avaient reçu le sérum de convalescent. Si nous relevons le jour de l'injection du sérum et celui du décès, par rapport au début de la maladie, nous obtenons ce qui suit:

N. de cas injectés	*Jour de l'injection*	*Depuis le début de la maladie* — *Jours du décès*										
		1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11e*
5	2e			2	1	1	1					
6	3e				2	2	2					
6	4e				1	3	2					
4	5e					1	1			1	1	
2	6e							1		1		
2	7e							1	1			
1	8e											1

Chez tous ces malades, la marche de la maladie s'est poursuivie sans arrêt vers le dénouement fatal: température élevée, le plus souvent sans aucune rémission; accélération constante du pouls; paralysie rapidement envahissante, aboutissant chez le plus grand nombre à des troubles respiratoires rapidement mortels. Cliniquement, j'ai eu l'impression que le sérum de convalescent modifie favorablement l'évolution des poliomyélites dont l'infection est de moyenne intensité: 1° lorsqu'il est administré à la période pré-paralytique, le plus près possible du début de la maladie; 2° lorsqu'il est administré dans les tout premiers jours qui suivent l'apparition de la paralysie; mais qu'il ne modifie nullement l'évolution des poliomyélites dont l'infection est immédiatement profonde et grave, que son administration soit précoce ou tardive.

SIALOLITHIASIS*

By C. H. Austin Walters, M.D., C.M.,

Belleville, Ont.

THIS study of salivary calculi was prompted by a case of spontaneous expulsion of a calculus from Wharton's duct reported below. A review of the literature by Harbeson[1] shows only 7 previously reported cases of spontaneous expulsion of the calculus in this condition, although he remarks that sialolithiasis itself is much more common than one would suspect. At present nearly 500 cases of sialolithiasis have been reported, so that one is forced to the conclusion that it is not uncommon, and not diagnosed as often as it should be. Because of its rarity compared to other calculi it is easily overlooked. The patients do not usually give a very definite history and the physician is not always alive to its possibility. Bailey,[2] in speaking of the submaxillary variety, calls it "the Cinderella of stones to which human secretory and excretory mechanisms are heir, owing its lowly position in surgical estimation to the fact it is never a cause of death, although it is the source of much pain and inconvenience." It must be remembered at this point that as long as a calculus is present anywhere in the salivary apparatus, acute spreading cellular infection is always a primary and serious consideration.

Etiology.—Calculi in the salivary apparatus occur most often in the submaxillary gland, next often in the parotid, and infrequently in the sublingual. At least 60 to 70 per cent of all cases are submaxillary, either in the gland or Wharton's duct. They are more frequent in males than females, and occur at all ages. Burdel[3] reports a case of sublingual calculus in an infant three weeks old. Salivary calculi vary greatly in size, ranging from minute particles up to two inches in circumference by one and a half inches long (the largest on record). Naturally, the gland variety is larger than the duct type. They are usually yellowish-white in colour, and cylindrical or spherical in shape. Nearly always the stone is single, but they may be multiple, especially in the parotid, where as many as fourteen have been found (Noehren[4]). In a submaxillary case thirty stones were obtained.

Their formation is due to a small foreign body lodging in the duct, or a plug of bacteria. Hence poor dental and mouth hygiene are contributing factors. The rest of the process is merely a precipitation of the salivary salts about the nucleus, since the salts found on chemical analysis in a calculus are always those occurring in the saliva. Their chemical composition is about 20 to 25 per cent of organic material, the greatest part being calcium phosphate and calcium carbonate, with traces of iron and magnesium.

Symptoms.—The symptoms are variable, and depend on whether the calculus is situated in the parotid or submaxillary glands, and on whether it is in the duct or the gland itself. Many patients have symptoms extending over years; others have no complaints until the stone exerts a ball-valve action, with blockage of the duct and resultant retention of the salivary secretion. In some cases, the patient can only remember feeling a hard mass against the mucous membrane of the mouth, appearing at intervals, or recurrent mild attacks of circumscribed tender swelling in the region of the involved gland, or having a disagreeable taste due to pus exuding from Stenson's or Wharton's duct, indicating a chronic inflammatory process in the gland itself.

Harrison[5] has written an excellent article, dividing the symptomatology into three groups. The first group comprises those showing the classical French "salivary colic", where just before or during eating the patient may have pain and slight swelling in the region of the involved gland. This is not common, however. The second group may or may not present recurrent local swelling, with a sudden attack of pain, fever, and a moderate leucocytosis. In these, chronic inflammation of the glandular tissue is present, and the existence of a cal-

* From The Boston Dispensary District Medical Service, Boston, Mass.

culus is sometimes hard to determine. The third group will show a board-like swelling, with the tissues fixed. In the submaxillary type the tissues beneath the tongue are fixed and very tender. In acute cases there can be severe pain in the ear and along the side of the cheek (parotid type); marked dysphonia and dysphagia, and pain in the tongue (submaxillary cases).

On examination, the calculus may protrude from the involved duct with local swelling, tenderness and redness, or it may be felt by palpation along the buccal membrane. It is best, however, to use bimanual palpation, *i.e.*, one finger in the mouth and one outside. If the calculus is in the duct it should be located in nearly all cases. Bimanual palpation is most easily done with the head flexed and inclined to the affected side in order to relax the musculature. X-ray will give helpful information in 70 to 85 per cent of the cases, although some calculi are very small and it is difficult to throw off superimposed shadows. In sublingual and submaxillary cases dental plates held by the teeth are most useful. Probing of the duct to determine the presence of a calculus is not recommended, on account of the danger of perforation and the spreading of an acute inflammatory process into the surrounding tissues. Besides, if felt by probing, palpation will reveal the diagnosis just as readily.

Differential diagnosis.—Sialolithiasis must be differentiated from all glandular swellings due to cysts and lues, acute inflammatory lesions such as epidemic parotitis and post-operative parotitis, actinomycosis, lymphadenitis from infected tonsils and teeth, increased calcification of the mandible, Mickulicz's disease, and malignancy of the cervical glands. The last involves, perhaps, the most important differential problem. One would be inclined to think of calculus where there are repeated acute attacks with intermittent swelling of the gland, especially if there is suppuration present and pus can be expressed from the opening of the duct. Also in calculus there is pain just before or during meal-time. In calculus, too, on bimanual examination the external swelling is continuous with the intra-buccal swelling.

Treatment.—In acute cases with marked swelling most authors advocate expectant treatment. This means putting the patient on a liquid diet, applying ice locally, using mouth washes, and waiting for the acute swelling to subside. Since Wharton's duct has no musculature, the pressure of the walled-up saliva within the gland aided by the musculature of the floor of the mouth must expel the calculus, if small enough. For this reason antispasmodics are of no value, general sedatives being more desirable. If the stone can be easily felt in the anterior two-thirds of the duct, slitting the mucous membrane over the stone, using 2 per cent novocaine locally, is the rational procedure. When in the posterior third of the duct use general anæsthesia. Removal of the gland in its entirety is advocated where there are multiple calculi and in cases of long-standing obstruction, which invariably lead to degeneration of the glandular tissue, owing to the chronic inflammatory process present, and where there is resulting stricture of the duct after dilatation methods have failed. In extirpation of the gland, if chronic inflammation is present, one avoids the danger of a resulting fistula. Always insert a small drain for the first few days.

REPORT OF THE SPONTANEOUS EXPULSION OF A SUBMAXILLARY CALCULUS

Mrs. J. W., a widow, white, aged 65, called the writer because of unilateral swelling along the mandible and pain radiating along the left side of the face and under the tongue.

Her past history showed nothing important except essential hypertension of several years' standing. During this time she had been treated at the Boston City Hospital for three "shocks". The last one was a year before, when she had a left-sided hemiplegia which had cleared almost entirely, the only neurological signs at the time of consultation being a slightly exaggerated knee jerk on the left side. It is possible these "shocks" were cerebral angiospasm. The blood pressure was 180/90. Under careful questioning, the only previous suspicious complaints of salivary calculus were a vague dull pain at long intervals radiating from the left temporal region down the left cheek to the under and anterior portion of the mandible, of four or five years' duration, and not bearing any relationship to the taking of food.

The illness started one week previous to her being seen, with moderately severe pain, beginning in the left ear and radiating down the left side of the mandible, particularly severe in the region of the submaxillary gland and below the tongue. This was accompanied by swelling under the mandible and below the tongue. These symptoms continued steadily for a whole week. A few hours previous to my visit the swelling under the tongue ruptured, and the patient expectorated a considerable amount of bloody purulent material and a stone. This was followed almost immediately by relief from pain.

Local examination showed a very firm, slightly tender submaxillary gland, the size of a small hen's egg. Just to the left of the frenulum linguæ there was a slit-like aperture, approximately 0.5 cm. wide, from which a slight amount of bloody purulent material was exuding. The opening was pouting and markedly injected, and the tissues about this firm and tender. The temperature was 98.4° and the pulse 84. The specimen preserved

was a calculus, fusiform in shape, yellowish-white in colour, and with a generally fine roughening of its entire surface. It was of fairly hard consistency, and did not crumble on pressure. It measured 1 cm. in length and 1.5 cm. in circumference.

After two days the purulent discharge ceased and for two more days Wharton's duct was still excessively prominent. The glandular swelling decreased slowly in size. After three weeks the gland was still slightly enlarged, but quite soft in consistency and not tender. On bimanual examination along the anterior two-thirds of the duct there was slight roughening felt, but skiagrams, taken from several different angles revealed no calculi. The patient is symptom-free at time of writing.

REFERENCES

1. HARBESON, *Canad. M. Ass. J.*, 1933, **28**: 537.
2. BAILEY, *Brit. J. Surg.*, 1925, **12**: 321.
3. BURDEL, *Comp. Rend. Acad. d'Sc.*, 1860, **1**: 893.
4. NOEHREN, *J. Am. M. Ass.*, 1923, **80**: 25.
5. HARRISON, *Surg., Gyn. and Obst.*, 1926, **43**: 431.

Case Reports

BILATERAL ACUTE MASTOIDITIS WITH LATERAL SINUS PHLEBITIS COMPLICATING THE COURSE OF AN ETHMOIDAL CARCINOMA*

BY R. P. WRIGHT, M.D., C.M., F.R.C.S.(C.) AND J. W. GERRIE, M.D., C.M.,

Montreal

Mrs. C.P., housewife, aged 63, was admitted by ambulance on December 12, 1932. She had had a low-grade, inoperable carcinoma of the left lateral nasal wall, maxillary antrum and ethmoidal labyrinth for seven years. On her first admission, five years previously, a fungating mass protruded from the left nostril and there was hard, indurated involvement of the left side of the nasal bridge down to the inner canthus of the eye. Biopsy at that time showed an epidermoid carcinoma of low-grade cellular activity. Deep roentgen-ray therapy was instituted and followed with interstitial and surface radium irradiations. The results were recession of the growth and relief to the patient. Further courses of deep roentgen-ray therapy were given as the progress of the growth indicated. The interior of the nose became clear, but widely ulcerated, and had a marked tendency to foul crusting, which was kept under control with Seiler's nasal irrigations.

Nine days prior to admission, the fourth of a series of roentgen-ray irradiations was given. That night saw the onset of an acute upper respiratory infection and the following day acute bilateral otitis media set in with spontaneous rupture of both drum-heads and profuse serous discharge. The ethmoidal growth became involved in the acute process, the external swelling increased, became red and angry and closed the left eye. Increasing deafness was a pronounced feature. She was first irritable, then drowsy, became markedly prostrated, and could no longer tend to her nasal hygiene.

Physical findings.—Temperature 99.6°; pulse 88; respirations 20. The patient was a well nourished elderly female, appearing miserable, flushed, stuporous, and little concerned in her surroundings. The carcinomatous growth was acutely inflamed, with swelling over the bridge of the nose and closing of the left eye which was bathed in pus. Internally, the previously ulcerated left lateral nasal wall and cribriform area were covered with a thick crusting, behind which was a foul pus. The remainder of the nose and throat was acutely congested. Marked deafness was present and the patient was unable to interpret the shouted voice. Tenderness was marked over the mastoid tip and antrum. Thin, yellow pulsating discharge came from anterior perforations in both drum-heads, which were red, bullatous, and showed shelving into the posterior canal wall. Leucocytosis was 10,300; corrected sedimentation velocity 2 mm. per minute; and the urine was normal. Roentgenograms, aside from showing a moderate sclerosis, were negative.

Progress.—The case was considered as an acute influenzal type, then prevalent in Montreal, involving not only both middle ears and mastoids but the cancerous nasal growth as well. Tough crustings were removed from the nose daily with liberation of foul pus. A paraffin spray failed to reduce the crusting. Ice was continuously applied to both mastoids and the ears irrigated daily. The ear condition continued acute, first the right ear being more markedly involved, but at the end of ten days the left had taken on a greater severity. On the 12th day after admission there was a sharp

* From the Ear, Nose and Throat Clinic of the Montreal General Hospital.

rise in temperature to 104° and the patient lapsed into a semi-stuporous condition. Four days later she had a chill and the temperature became markedly hectic, fluctuating between 104° plus and 97°. Blood culture was negative. The differential points at issue were whether the septic absorption was coming from the cancerous growth via the cribriform area, or through the mastoids into the lateral sinuses, and, if the latter, which side was offending. Following staff consultation, it was deemed advisable to open the left mastoid and expose the lateral sinus. This was done on the 18th day after admission. The mastoid cells and antrum were essentially normal, there being no free pus or breaking down. However, the sinus was exposed and showed a slightly yellowish hue in the centre but appeared normal at both ends and was soft and fluctuant throughout. It was not considered sufficiently abnormal to warrant opening. The patient was returned to the ward, the focus of absorption being still a matter of conjecture as the nose was still crusting heavily, walling up large amounts of pus, and the other ear still involved in an acute process. The hectic condition continued, the patient becoming stuporous and incontinent. Because of first the irritability followed by drowsiness, incontinence, etc., the possibility of frontal lobe abscess was being considered. However, the optic discs were normal and there were no pathological reflexes. Three days later, lumbar puncture showed a pressure of 180 mm. of water; clear fluid; negative Pandy, 10 cells; and the pressure rising to 230 and 250 mm. on right and left jugular compression respectively. Packing was removed from the mastoid wound and the sinus still appeared soft and healthy aside from a slight yellowish discoloration in the centre. On the 5th day following the mastoidectomy, the left jugular vein was tied off and the sinus collapsed, this treatment being considered, at the time, preferable to mere opening and packing off the sinus. It contained fluid blood throughout. There was a dramatic fall in temperature and an amelioration of all symptoms, the patient sitting up seven days later with progressive, uneventful recovery.

COMMENT

The case was evidently one of a septicæmia, with absorption from the left lateral sinus, of more than passing interest because of the many confusing points—whether absorption was from the infected carcinomatous growth *via* the ethmoidal veins and cavernous sinus, or from the mastoids *via* the lateral sinuses, and, if the latter, which sinus? The insignificant findings in the left mastoid and lateral sinus, negative blood cultures, and the possibility of brain abscess further confused the clinical picture.

TRAUMATIC RUPTURE OF THE BOWEL

BY J. EDGAR WILLIAMS,

St. Mary's, Ont.

L.B., a male, aged 20. While engaged in the razing of a barn, this young man and another workman were struck, each on the chest, by a swinging beam. The other workman managed to cling to a support, and escaped with two fractured ribs; L.B. fell about twelve feet, striking the edge of an open hay chute. When seen about a half hour after the accident, the patient was obviously suffering from shock, but complained only of pain in the left chest, the pain being aggravated by deep breathing. Both he and his companion were treated for fractured ribs and put to bed.

About two hours later he began to have pain in the lower abdomen over the bladder area. Severe pain occurred in spasms, and a continuous aching pain in the same area. He had passed clear urine since the accident. No nausea or vomiting had occurred.

The patient was pale, his temperature normal, his pulse rapid at 90, but of good tone. Examination of the abdomen showed very little movement on respiration, and revealed tenderness and slight rigidity over its lower third. A shifting dullness in the flanks indicated the presence of free fluid in the peritoneal cavity.

A diagnosis of ruptured intestine was made, and the patient removed to hospital. At operation, seven hours after the accident, the abdomen was opened over the seat of the pain, through a left para-medial incision, and the injured loop of small bowel almost immediately discovered. A perforation, the size of a lead pencil, was found on the free side of the small bowel, blood and intestinal contents being free in the peritoneal cavity. The hole in the bowel was closed by suture. As much as possible of the fluid was removed by suction, and about ten ounces of bismuth emulsion poured in. The abdomen was

closed without drainage. The patient made a good recovery, being on his legs within two weeks.

That rupture of the bowel will occur as a result of a blow on the abdomen, the wall of which shows no evidence of injury, should always be kept in mind, since prompt surgical intervention is the only method of saving life in such a case.

ECZEMA TREATED BY ADRENALIN

By Carman C. Browne,

Nanaimo, B.C.

I would like to report on an eczematous condition which I developed some weeks ago and which yielded to a treatment which I have not heard of being used before.

Two weeks ago I developed a small area of eczema on my face which gradually increased to the size of a fifty cent piece. The area was very itchy and exuded considerable serum which formed unsightly scabs. When these were removed a raw red surface was exposed, followed by much discharge of serum. The condition was little improved by the application of calamine lotion and zinc oxide ointment, and daily quartz-lamp radiations. The latter seemed only to aggravate it.

Considering that there was a similarity in the causation of urticaria and eczema, I decided to try the effects of adrenalin. Four or five applications were made several time a day. After each series the eczematous area became quite pale and in twenty-four hours a distinct improvement was noted — the coagulated serum could be removed easily at the periphery, and on so doing little or no serum was formed afterward. The applications were continued for several days. There was no more itching, and finally the coagulated serum was all removed with the aid of zinc ointment at night. The raw area was always painted with adrenalin immediately after the removal of the scabs.

Comment. — The application of adrenalin would seem to be a rational method of treatment of the "weeping" type of eczema. So much serum exudation suggests an increased permeability of the capillary walls. (As heat is a vasodilator this explains the deleterious action of the quartz-lamp).

The immediate blanching of the rash area and the inhibited exudation prove the value of the vasoconstricting properties of adrenalin in this condition.

A CASE OF UNDULANT FEVER

By J. H. Grove,

Paisley, Ont.

Mr. J.G., aged 46, began to complain of chills and weakness during the last week of March, 1933. He felt feverish the first week of April. I saw him on April 5. Temperature 103°; pulse 100. The patient was pale, sweating, slight cough, pain in back, diagnosis influenza. As he lived 10 miles away, I did not see him again till he sent for me on April 15th. Temperature then was 103.2°; pulse 100. He did not feel very sick, ate well, sweated profusely, had pleurodynia and a hacking cough, but nothing else abnormal was noted. He had some spots on the skin that looked like rose spots, but as the temperature became normal, I did not think he had typhoid. After several days' normal temperature, a continuous fever set in. He did not feel sick, ate well, but had pain in the left upper quadrant of abdomen. Bowels, kidneys and chest, normal.

About May 1, 1933, he did begin to feel very ill and became delirious. A blood test showed agglutination for *B. abortus*. On May 5th, I sent for *B. abortus* serum supplied through courtesy of the Animal Research Institute, Hull, Que.

May 6th, temperature 104.4°; pulse 110. Patient looked the picture of severe typhoid fever. I injected 1 c.c. *B. abortus* serum intramuscularly. Next day the temperature was 102.2°; pulse 110; 2 c.c. serum were given; the patient felt better and began to eat again.

May 8th, temperature 101°; pulse 108; 3 c.c. serum injected.

May 9th, temperature 100°; pulse 104; 4 c.c. serum injected.

May 10th, temperature 100°; pulse 100; 10 c.c. serum injected.

May 11th, temperature normal; patient felt well again; no pain, no sweating, good appetite. Since then he has had no elevation of temperature and is now up and about, though still a bit weak.

The abortus anti-serum used in the case had an agglutination titre of 1:100,000. The titre of the patient's blood after treatment was 1:640,

positive, and 1:1280, partially positive (report from the Animal Diseases Research Institute).

I know that some critics will say and have already said that the recovery in this case was just a characteristic of the disease, but the response was too dramatic. I cannot believe that a patient so desperately ill could recover by a natural process so rapidly. Moreover I understand that other favourable results from the serum have been reported since then. In addition, the extremely high titre of the serum used should be taken into consideration. However, I am not qualified to offer opinions or explanations. All I know is the patient was extremely ill, I injected the serum and he almost immediately began to get better, and in several days all the symptoms attributable to his infection had disappeared. He was weak, of course, but he said he felt well enough to get out of bed if I would let him.

Editorial

AMIDOPYRINE AND THE BARBITURATES AS POSSIBLE CAUSES OF GRANULOCYTOPENIA

AGRANULOCYTOSIS, better called "granulocytopenia", while not altogether a common disorder, is occurring with sufficient frequency to merit careful attention on the part of the clinician, and, further, as it is highly dangerous to life any new light on its etiology is welcome.

Authorities who have studied this remarkable affection are, apparently, not in agreement as to whether it should be regarded as a primary disorder of the bone marrow or, again, as secondary to some extraneous toxic agent acting on the bone marrow. What evidence we possess at the moment suggests that the latter view is correct, at least in the great majority of cases. Thus, granulocytopenia is frequently to be linked with the activity of benzene, toluene and coal-tar products, and with the exhibition of radium and the x-ray. Recent work draws attention to the possible toxic action of amidopyrine (pyramidon), the barbiturates and sanocrysin in this connection. The observations referred to are, if not conclusive, at least highly suggestive.

Doctor Watkins,[1] of the Mayo Clinic, reports 32 cases of agranulocytosis. Twenty-four of the patients had taken either amidopyrine or a barbituric acid derivative for varying periods before the onset of the trouble; eight gave no history of having taken any drug previously. Two died out of ten who had taken amidopyrine and developed granulocytopenia. One who recovered had had twelve attacks of granulocytopenia in two years and a half, each after using amidopyrine. Two other patients had taken a mixture of amidopyrine and dial; they recovered. Five had taken amytal (isoamyl-ethyl-barbituric acid) or its sodium salt before the onset of the granulocytopenia and all died. One patient, dying in her second attack, had taken a mixture of allonal (allylisopropyl barbituric acid) and amidopyrine. Four patients had taken nembutal (sodium ethyl-methyl-butyl barbiturate) and all died in their first attack of granulocytopenia. Two patients had taken luminal (phenyl-ethyl barbituric acid), of whom one died, but in this case there was an overwhelming infection which may have accounted for the granulocytopenia. In commenting on these cases, Dr. R. D. Gillespie[2] remarks "some details have come to me privately of the paper as it was actually read in Chicago, from which it is evident that the majority of these patients were physically ill in some way or another at the time—in fact all except one of them of which I have a record; moreover all of them had several doses on successive days of either amidopyrine or a barbiturate or both combined." Watkins's own comment is as follows:—"I do not feel that the cases here considered prove that amidopyrine or derivatives of barbituric acid are etiologic factors in producing granulocytopenia, but I do believe that it is a possibility that certain individuals have an idiosyncrasy to the drug which is

1. WATKINS, Proc. Staff Meetings, Mayo Clinic, Nov. 22, 1933, p. 713.

2. GILLESPIE, R. D., *The Lancet*, 1934, **1**: 344.

manifested by granulocytopenia. If this is an idiosyncrasy it must be exceedingly rare, for enormous numbers of people use the drugs considered without known untoward reaction. A great deal of clinical and experimental evidence will be needed to establish this thesis." This position is eminently cautious. Watkins, in the paper referred to, mentions the earlier paper of Madison and Squier, who reported a series of thirteen cases of granulocytopenia in 1933, which they concluded were probably due to the use of members of the benzene group.

More recently, Madison and Squier,[3] following up their earlier observations, have reported on fourteen cases of granulocytopenia, together with some experimental work. Each of their cases followed the use of amidopyrine, either alone, in combination with a barbiturate, or combined with other drugs. In eight cases the further use of amidopyrine was prohibited and only two of the patients died. In the other six, owing to the fact that no harmful effect was suspected, amidopyrine was used for the relief of pain and restlessness and all the patients died, in spite of the fact that four of them recovered from the acute attack.

To these clinical observations the authors add others derived from direct experimentation. Two patients who had recovered from an acute attack were given, the one 0.3 g. of amidopyrine, and the other, 0.45 g. of amidopyrine with 0.2 of amytal. In both cases, and within a few hours, a transient marked depression of the granulocytes occurred. Eleven rabbits were given either allonal or amidopyrine alone. One rabbit, which had received a daily average of 1.3 g. of amidopyrine, manifested on the twenty-fifth day a sharp drop in the number of the granulocytes, which progressed until death occurred on the thirtieth day. Before its death this animal exhibited a complete absence of granulocytes in the blood, and, after death, no granulocytes could be detected in the bone marrow. Seventeen other rabbits, given either allonal or amidopyrine, showed no significant alteration in the blood picture.

We may add to this that Kracke[4] found that subcutaneous injection of benzene and olive oil in small amounts could produce agranulocytosis in rabbits, though he did not succeed when he gave amidopyrine by the mouth or by injection.

It would seem that Madison and Squier have made out at least a *prima facie* case for their conclusion that granulocytopenia may follow the use of amidopyrine, either alone or combined with a barbiturate, though they think that the persons so affected exhibit a special idiosyncrasy; in other words, that granulocytopenia in these cases is an example of an allergic drug reaction. It is suggestive, too, as they have noted, that the affection is found commonly in persons who are most likely to be taking drugs—physicians, nurses and those directly under the care of a physician. This is, of course, not the whole story, for granulocytopenia has often enough been found in persons who have not been taking the particular drugs incriminated.

More recently still, Hoffman, Butt and Hickey[5] have brought forward corroborative evidence. In six to eight years Hoffman has had occasion to treat fourteen cases of agranulocytic angina. All of these died but one. The exception, a woman who had taken dinitrophenol for reduction purposes, recovered after the use of x-rays and pentnucleide. On going back to the histories of the twelve fatal cases observed up to August, 1933, Hoffman was astonished to find that all of these patients had been taking amidopyrine, either alone or in conjunction with codeine for the relief of pain. A few had received some barbitural products, such as phenobarbital, pentobarbital or isoamyl-ethyl barbituric acid. None had taken allonal. Subsequently an additional case was observed—a man who had received 75 grains of amidopyrine during 36 days for headache died in somewhat under six weeks with granulocytopenia, in spite of vigorous treatment with pentnucleides and liver extract. His leucocytes dropped to 450 per c.mm., and the neutrophiles entirely disappeared. In their experimental work, Hoffman, Butt and Hickey used only amidopyrine, in rabbits. Doses of this drug, varying from 0.2 to 0.9 g. per kilo given by mouth produced definite leucocytosis

3. MADISON, F. W. AND SQUIER, T. L., *J. Am. M. Ass.*, 1934, **102:** 755.

4. KRACKE, R. R., *Am. J. Clin. Path.*, 1932, **2:** 11.

5. HOFFMAN, A. M., BUTT, E. M. AND HICKEY, N. G., *J. Am. M. Ass.*, 1934, **102:** 1213.

followed by leucopenia, and in some of the rabbits the proportion of granular leucocytes was reduced as low as 8 per cent. The common factor in benzene, amidopyrine, dinitrophenol, arsphenamine, ortho-oxy-benzoic acid and hydroquinine, all of which have produced neutropenia experimentally and clinically, is the benzene ring. Whether the latter is the actual toxic agent or not requires further study. The work of Hoffman, Butt and Hickey points to amidopyrine having a definite effect on myeloblastic tissue, similar in man and in rabbits. Whether this is an allergic reaction or not also remains to be determined.

Dr. N. Mutch, Physician to Guy's Hospital and Lecturer in Pharmacology in the University of London, gives a useful Table[6] of some of the commonly used proprietary preparations which contain amidopyrine, most of them being compounded with one of the barbitural series:—

Analgesics based on Amidopyrine

Allonal	=	Amidopyrine	— a barbiturate
Asciatin		"	— butyl chloral
Cibalgin		"	— a barbiturate
Compral		"	— a urethrane
Optalidon		"	— a barbiturate
Somnosal		"	— bromural
Veramon		"	— barbitone
Veropyron		"	— barbitone

Watch these.

In the light of the observations above referred to it would seem that amidopyrine is the chief offender, but the barbiturates are not free of suspicion. The coal-tar derivatives as a whole will bear watching. The points in doubt can only be cleared up by the careful study and recording of all cases of granulocytopenia, with particular reference to a history of the taking of drugs which are in any way likely to be at fault. More evidence is called for and the clinician can do much in this regard.

A.G.N.

6. MUTCH, N., *Brit. M. J.*, 1934, **1**: 321.

BRUCELLA ABORTUS AND UNDULANT FEVER IN MAN

AN article in this issue by Dr. Redvers Thompson[1] serves once again to call attention to a subject that is of great importance to the community. Undulant fever in man is by no means rare in Canada, as we have learned; cases have been recorded at intervals since 1928, both in our own *Journal* and in the *Public Health Journal*. More than five hundred cases have been reported in Canada during that period. Infection of cattle with *Brucella abortus* Bang is quite common in this country also; Doctor Thompson states that twenty per cent of the dairy cattle are thus affected—a somewhat disconcerting thought. Goats and swine are also infected with organisms of the Brucella group, but, apparently, to a less extent.

Much has been learned about the organisms now grouped together under the generic name *Brucella* since Bang[2] discovered his *Bacterium abortum* in 1897 and Bruce[3] the *Micrococcus melitensis* in 1907. Alice Evans,[4] working in 1918, considered that these two forms were indistinguishable morphologically, biochemically and culturally, and, moreover, were closely related serologically. We are now able, however, with more refined methods of cultivation, to make a distinction between *Brucella melitensis*, as Bruce's organism is now called, and *Brucella abortus* Bang; the former will grow in the presence of oxygen; the latter requires an atmosphere of CO_2. At the present time cultural methods are much more trustworthy, speaking from the standpoint of diagnosis, than is the agglutination test. A positive culture indicates a present infection; a positive agglutination test has the same value as the Widal test, no more, no less, that is, it may indicate an active process; or it may only point to a previous infection from which the host has recovered, or to a "carrier" state. The agglutination test will usually distinguish between *Br. melitensis* and *Br. abortus*, but not between the bovine and porcine strains of the latter. The former part of this statement is exemplified in two cases reported in this *Journal*[5] by Drs. M. R.

1. THOMSON, R., *Canad. M. Ass. J.*, 1934, **30**: 485.
2. BANG, B., *Deutsche Zeitschr. f. Thiermed.*, 1897, **1**: 241.
3. BRUCE, J., *J. Roy. Army Med. Corps*, 1907, **8**: 225.
4. EVANS, A., *J. Inf. Dis.*, 1918, **22**: 589.
5. STALKER, M. R. AND ROSS, J. B., *Canad. M. Ass. J.*, 1930, **23**: 62.

Stalker and J. B. Ross. The first gave a positive agglutination against *Br. abortus* up to 1:1250 as against *Br. Melitensis*, 1:20; the second was positive against *Br. abortus* up to 1:500 as against *Br. melitensis*, 1:10, only. As indicating the persistence of a positive agglutination reaction, it may be stated, in passing, that the latter patient had had what was probably undulant fever six years before.

The idea that undulant fever in man is closely related to contagious abortion in cattle was first advanced by Bevan, of Rhodesia, in 1922 and in 1924 Keefer[6], for the first time, proved the *Br. abortus* to be the cause in a case of undulant fever in the human subject. Since that date the organism of Bang has been fairly frequently isolated from the blood in human cases of undulant fever, doubtless owing to improved methods of technique. Doctor Thompson, in his paper herein published records, for the first time in Canada, the isolation of *Br. abortus* from the blood in a case of undulant fever in the human subject. In view of all this, there is no doubt at all that *Br. abortus* is pathogenic for man, a view that, some few years ago, at least, was doubted. Indeed, it is safe to go farther and say that this organism is the usual cause of undulant fever in Canada, for goats are not nearly so frequently kept as are cattle. Pigs may be a source of infection, either directly, or indirectly through cattle, for the strains of *Brucella* found in these animals are more closely related to each other than either of them is to *Br. melitensis*, and these animals can be reciprocally infected by each other's organisms, but, again, pigs are not so common as cattle. The danger to the human subject in Canada comes mainly from milch cattle and dairy products. At the same time, while we must conclude that *Br. abortus* is competent to produce in man all the clinical features usually regarded as characteristic of undulant fever, this statement should be qualified by the further consideration that its infectivity is high but its pathogenicity is rather low. That this is the case is supported by the fact that while twenty to thirty per cent of the raw milk sold in Great Britain has been shown to contain *Br. abortus* undulant fever appears to be uncommon[7]. Also, in Canada, as in Great Britain, a considerable number of persons give a positive agglutination test who have never had undulant fever, and the mortality from undulant fever is not high. Possibly, however, undulant fever is a disease that is struggling for recognition, as it were, and all this may some day be changed.

Cases of human infection are, as is now well recognized, due to contact with infected cattle or their dejecta and to the use of milk and milk products derived from infected animals. The danger is all the greater because such animals need not be ill; they may simply be "carriers" and their rôle unsuspected. Thompson[8] has isolated *Br. abortus* from ice-cream, and has pointed out the danger of using ice-cream made from unpasteurized, "certified" and "special" milk. Carpenter and Boak[9] have found that the organism may remain viable in butter for 142 days at 8°C., and Voille,[10] in cheese for two months. Herein is another argument in favour of compulsory pasteurization for *all* milk, if any be needed.

A.G.N.

6. KEEFER, C., *Johns Hopkins Hosp. Bull.*, 1924, **35:** 6.
7. *The Lancet*, 1934, **1:** 692.
8. THOMPSON, R., *Canad. M. Ass. J.*, 1933, **29:** 9.
9. CARPENTER, C. M. AND BOAK, R., *Cornell Veterinarian*, 1928, **18:** 204.
10. VOILLE, La Fièvre Ondulante, Masson et Cie., Paris, 1931.

DYSENTERY: REPORT OF THREE CASES IN ONE FAMILY DUE TO ATYPICAL BACILLUS DYSENTERIÆ AND ENDAMŒBA HISTOLYTICA. — Weinberger presents three cases of amœbic dysentery in which infection occurred in Chicago and believes that the possible cause for the failure to find *Endamœba histolytica* early in the recently reported fatal cases of acute dysentery in the late epidemic was the relatively long incubation period of this parasite. *Bacillus dysenteriæ*, described by Schorer and Duval in 1904, was isolated in the author's cases sixty days before the discovery of *Endamœba histolytica*. Vaccine made from the isolated *Bacillus dysenteriæ* proved effective in the treatment of these cases, resulting in complete abatement of signs and symptoms until relapse, at which time *Endamœba histolytica* was found. *Endamœba histolytica* was discovered sixty days after the acute onset. The combination of emetine and chiniofon proved effective against the amœbiasis. In every case of acute colitis, the possibility must not be overlooked of the presence of double infection, especially the association of *Endamœba histolytica* with one of the *Bacillus dysenteriæ* group.—*J. Am. M. Ass.*, 1934, **102:** 916.

Editorial Comments

The Honourable Minister of Sports

Newspaper readers were treated to a rather unusual and interesting news item a few days ago. Some of them were perhaps amused. The article referred to was a resolution sponsored by the Canadian Bicycle and Sports Goods Association at its seventeenth annual convention in Toronto. It reads as follows:—

> "Resolved that this Association bring before the Legislatures, both of the Dominion and of this Province, the desirability and feasibility of including in their Cabinets a Minister of Sports and Recreation whose Department would specialize in the promotion of a more active participation in games and recreation by the people of the Dominion of Canada."

Whoever heard tell of such an idea! Just like a cyclist to think of such a scheme! Imagine a dignified Cabinet Minister as Minister of Sports!

But, wait a minute. When one examines this idea a little more closely and reflects upon it, perhaps it is not so ridiculous after all. Let us consult the pædiatricians, the mental hygienists, the neurologists, the psycho-analysts, the technocrats, the industrialists, the Chambers of Commerce, the captains of finance, the labour organizations, and what a consummate picture we shall get when we put all their opinions together. From the moment a child is born, its play time, in relation to habit formation, becomes a matter of some concern. The pre-school child is taken to the Nursery to be taught how to play intelligently. Primary and secondary schools are devoting more and more attention to the most appropriate methods to be employed in the utilization of school children's leisure time. In the holiday season, camps for girls, camps for boys, play grounds for the less affluent, organized games and sports, are everywhere to be found to take care of the leisure time. And then we come to our busy business and professional men. Golf clubs have multiplied by leaps and bounds, and represent an investment in Canada of millions of dollars; and along come the genii of the species and, overnight, they produce a robot which when operated by one man perhaps knocks fifty others out of employment. The artisan today is puzzled to know what to do with his time. Of course he wants a job with remuneration, but, even if he finds such a job, he is still going to have a lot of time on his hands. Now we come to the twilight and sunset period in life, and we simply must know how to play, or the old machine will quickly go to pieces and die, or, at least, so the psychologists tell us.

Well, is it not high time we had our Honourable Minister of Sports? And what a superman he should be—acquainted with child problems, labour problems, psychology, philosophy, and everything else that enters into human relations. One can see him sitting at the manual of his order board. He presses a few keys here, a few there, and, presto, one hundred thousand children are set loose to play under proper supervision; three hundred thousand artisans are turned out on our fifty thousand municipal golf courses, and, as they chase the little pill around, peace and joy come into their souls, replacing all irony and grumblings with regard to the meanness of fate which did not make them all bankers. The Honourable Minister of Sports is going to find his task increasing in the reverse ratio to man's scientific progress. We are going to work less and less, and play more and more, and when Utopia is reached the first Cabinet to be chosen will be from the Honourable Ministers of Sports. Should we not get on with the job at once and waste no further time in seeing that our Governments are immediately seized with the desirability of reconstructing their Cabinets at the earliest possible date? This writer is certainly all in favour of the bicyclists' resolution.

T. C. ROUTLEY

Recognition of Specialists in Medicine

The rapid trend toward specialization in medicine and the spread of small hospitals all over the country, with the opportunities thus provided for the undertaking of highly technical procedures, have resulted in frequent demands in both medical and hospital circles that some measure of control, some hallmark of approval, be instituted for the guidance of the public. Here in Canada the various British post-graduate degrees have been highly respected; the American College of Surgeons has done a great deal to raise the standards of surgery and general hospital practice and, more recently, the establishment of the Royal College of Physicians and Surgeons of Canada has laid the foundation for a high standard of scholarship. One province actually controls through a Board the issuance of specialty certificates, and now within the last few months the formation of the Advisory Board of Medical Specialties in the United States has contributed another solution to this problem which, inasmuch as any such procedure cannot but have a definite influence on Canadian medicine, may be of interest to the profession here.

The Advisory Board for Medical Specialties has been set up to assist in the coordination of the education and certification of medical spe-

cialists. It is made up of representatives of the American Boards of Ophthalmology, Oto-laryngology, Obstetrics and Gynæcology, and of Dermatology and Syphilology; the Association of American Medical Colleges, the National Board of Medical Examiners, the Federation of State Medical Boards, the American Hospital Association, and the Council on Medical Education and Hospitals of the American Medical Association. Examining boards in other specialties may be eligible for representation on this Board upon meeting certain high standards of qualification. The application of the American Board of Pædiatrics has been favourably approved and applications from other specialty boards are now under consideration.

The influence of this joint Board should be far-reaching. Many of the specialty societies are showing careful discrimination in the selection of their members; an increasing number of specialists are taking their respective Boards and many Canadian practitioners are included among the applicants. Specialty Boards will be required to give ample proof of their insistence that applicants be highly qualified before such Boards will be admitted to membership; this should be of real value in several special fields. The cooperation of the national and state medical Boards of Examiners indicates a close linking up with licensing bodies; the backing of the American Medical Association implies the hearty endorsation of organized medicine; and the participation of the leading hospital organization indicates the desire of the hospital field for the establishment of some reliable basis of approval whereby directors of services and appointees to other posts of responsibility may be selected. The profession in Canada will follow this development with considerable interest.

HARVEY AGNEW

Bulletin of the International Association of Medical Museums

We note that the *Bulletin of the International Association of Medical Museums* has decided to carry out the following policy. First, to limit its publications entirely to technical methods of medical museums. So far they have included papers of pathological interest, but feeling that these are best taken care of by pathological journals, especially from the point of view of indexing articles, they will henceforth confine themselves to the field denoted by the name of the Association, which it may be noted is not cared for in any other journal. The second point is that the *Bulletin* will be published regularly once a year. This will undoubtedly add to its usefulness as well as increase the activity of the Association it represents.

H.E.M.

The Association Booklet

We have before us the very informative booklet prepared by the Publicity Committee for the Annual Meeting of our Association to be held at Calgary in June. This committee, of which Dr. George A. Anderson is the efficient Chairman, have produced a work of which they may well be proud. Beautifully printed on good paper, and effectively illustrated, not too large, not at all "wild and woolly", we catch here, nevertheless, the free spirit of the West. Those of us who hail from the East may learn many things that will come as a surprise. It is hoped that the many attractions of Calgary will prove an incentive for all to make for the "City of the Foothills" next June.

The Booklet begins with a Message from Dr. J. S. McEachern, the President-elect of the Association, embellished with his portrait. All Members of the Association will rejoice to hear that the genial Doctor is making steady progress, if slow, in his convalescence from a serious illness. We sincerely hope that when the time comes Doctor McEachern will be able to assume the duties of his high office.

Then comes a "Song of the West", by Miss Marion E. Moodie, which simply and delightfully expresses the love of the Westerner for the West. We have the history of Alberta and Calgary, a description of the hospitals, an account of the worship of music, painting, and literature — all the fine arts — to which the Calgarians are devoted. Religion, education, agriculture, and economic development are also dealt with in brief effective articles. Lastly, we must not forget to commend the illustrations, two of which are in colour. The "Lure of the West" is in this booklet.

A.G.N.

A Reprint of "William Dunlop"

Many of our readers will remember the delightful sketch of William Dunlop, written by Colonel F. S. L. Ford, C.M.G., M.D., of Toronto, which appeared in the *Journal* of August, 1931. This article gave a graphic account of an important man who lived in stirring times. Colonel Ford has received so many requests for copies that he has had the article reprinted and it appears in a very pleasing dress. It takes the form of a small octavo pamphlet of sixty pages in a blue paper cover and is well printed and illustrated. Copies can be obtained on application to Colonel Ford or to the publishers, The Albert Britnell Bookshop, Toronto.

"Kelpekoe", a Recently Advertised Remedy for Diabetes

The Association has been asked several times lately for information as to a product known as "Kelpekoe", which is being advertised as a cure for diabetes. From the name one would infer

that the remedy is derived from the well-known seaweed called "kelp". Apparently, this is not so. A course of treatment lasting sixty days, at the low cost of $10.00, is said to be sufficient to cure diabetes. A letter to the Bureau of Investigation of the American Medical Association has brought us the following information from Dr. Arthur J. Cramp, the Director:

"We have not yet felt justified in going to the expense of analyzing Kelpekoe. The stuff has been on the market for some time and was earlier known as 'Pacific Health Ore', marked by the Pacific Health Ore Company of Salem, Ore.

"The stuff has been advertised for various conditions. In 1932 they were stressing its alleged virtue as a rejuvenator. In 1932, also, they were attempting to sell stock, and in their prospectus estimated that they should net a profit of from $50,000 to $100,000 a month. In the prospectus they reproduced a purported analysis made by the Bowser-Morner Testing Laboratories of Dayton, Ohio, which showed the chief ingredients to be aluminium sulphate (about 5 per cent) and ferrous sulphate (about 2½ per cent), with about 2½ per cent of organic matter.

"Also, according to the same stock-selling prospectus, Kelpekoe was said to be a 'natural deposit of highly mineralized blue shale'. The company claimed that it had sufficient ore to assure continuous output for many years and that they were selling it at $9,700 a ton.

"The idea of exploiting this nostrum as a cure for diabetes seems to be a comparatively recent one.

Very sincerely yours,

(Sgd.) ARTHUR J. CRAMP."

Medical men can draw their own conclusions.

A.G.N.

Special Articles

THE INDIAN TUBERCULOSIS PROBLEM AND SOME PREVENTIVE MEASURES*

BY R. G. FERGUSON, M.D.,

Fort Qu'Appelle Sanatorium,

Fort San, Sask.

In 1931 among the Indian population of Canada there were 672 deaths from tuberculosis, a death rate of 546.72 per 100,000. This death rate from tuberculosis is seven and one-half times the average for the total population of Canada. The general death rate among the Indians of Canada for the same year was less than twice that of the entire population. In the Province of Saskatchewan in 1931 the Indian tuberculosis death rate, using the census population of 1931, was 517.42 per 100,000, or fourteen times that for the total population of Saskatchewan.

The information derived from research studies carried on during the past six years by the Department of Indian Affairs, the National Research Council of Canada, and the Saskatchewan Anti-Tuberculosis League, supported by the experience of the Qu'Appelle Indian Health Unit during the past three years,† has made possible the proposal of a program for prevention and control in Saskatchewan, varying according to conditions, which it is considered will be both practical and economical.

The annual examination of Indian children in two schools on the Qu'Appelle Indian Research area for the past six years has demonstrated that the age of maximum morbidity in this group is between 10 and 14 years. During these years it attains an incidence more than ten times that of the white population in the same age group. This is the period when the children are actually attending the boarding schools. The boarding schools, therefore, are the strategic battle grounds for the control of tuberculosis among the Indians.

In the boarding schools environment and living conditions are under control, and a standard of sanitation can be maintained. In the Province of Saskatchewan approximately two-thirds of the Indian children attending school are at present being educated in government boarding schools, and when it is recalled that the children enter these schools at the age of 6 to 7 years and remain there until 16 or 18 years old, during which period infection with tuberculosis becomes almost universal, you may realize the opportunity that is afforded for maintenance of health and increasing resistance against tuberculosis in this controlled environment.

If all children with lesions were identified on admission and were removed from the boarding schools, other things being equal, a result approximating that which has been secured at the File Hills Boarding School, where only one breakdown has occurred during the past six years, might be anticipated for the remainder of the boarding schools in Saskatchewan. Few children would develop tuberculosis after admission to the schools, and when they became infected while in the schools the degree of infection would be sufficiently small to assist them in developing greater resistance.

* An abstract of a paper in the Transactions of the Twenty-Ninth Annual Meeting of the National Tuberculosis Association, being an account of an investigation being carried on by the National Research Council of Canada, the Department of Indian Affairs, and The Saskatchewan Anti-Tuberculosis League.

† (a) "Tuberculosis among the Indians of the Great Canadian Plains", Trans., Fourteenth Ann. Con. of Nat. Ass. for the Prevention of Tuberculosis, 1928.

(b) Reports, Qu'Appelle Indian Research to the Associate Committee on Tuberculosis, National Research Council of Canada, 1930, 1931, and 1932.

Observation over a period of six years has proved that when well nourished afebrile spreaders are retained in the schools, as has been done at the Qu'Appelle Indian School, an average of one pupil each year among those absolutely negative on admission has developed demonstrable tuberculosis, not to mention the possibility of reinfection in the case of others who have broken down.

For the past six years the second highest mortality among the Indians of Canada was found in the age period of 15 to 19 years, the rate being 772.47 per 100,000, the corresponding rate for Saskatchewan being 928.91 per 100,000. It is hoped that in future when these young adult Indians are discharged from the schools at an average age of sixteen in good health fewer will be found to develop the disease during the next decade, after which tuberculosis among the Indians quickly approaches the mortality of the white people.

Healthful schools and healthy school children would mean less infectious parents for the succeeding generation, less massive infection, and a much lowered mortality from tuberculosis among infants, in which group we now find the highest mortality from this disease. This group will also receive special consideration in the program, as will be seen later.

The preventive measures that are being instituted for the boarding school problem in Saskatchewan for the purposes of demonstration are:

1. A selective x-ray and physical examination of the Indian school children throughout the province, as soon as possible after the opening of the schools in the autumn.
2. As previously, the exclusion of the children actually sick.
3. The segregation of the tuberculous children who, though showing lesions, are still well nourished, in a school set aside for their education and care, at a cost little more than an average boarding school. These children in the past have been retained in the schools as "spreaders".
4. The elimination of bovine tuberculosis from the dairy herds of the boarding schools and from any reserves where raw milk is being used.
5. The intensive education of these children in matters of sanitation.
6. The application of general health principles in these schools.

Secondly, there is the pre-school problem, that of caring for infants and children in an uncontrolled environment where a large percentage of the families are tuberculous and where the tuberculosis death rate among infants is tremendous. During the past six years in Canada the average tuberculosis death rate among infants up to one year has been 1018.39 per 100,000, and the corresponding rate for the Indian infants of Saskatchewan has been 1603.49. Where both protection against infection by isolation and improvement in sanitation must await the progress of the evolution of a primitive race, the change, however stimulated, will be slow.

TABLE SHOWING THE AGE INCIDENCE OF MORBIDITY AND CALCIFICATION ON THE QU'APPELLE INDIAN HEALTH UNIT, 1930-1931

Age groups	*Number in each group*	*Total active tuberculosis*		*Total inactive tuberculosis*		*Total calcification*	
		No.	*percentage*	*No.*	*percentage*	*No.*	*percentage*
Under 1 yr.	25	..	..	..	..	3	12.00
1 – 4 yrs.	115	7	6.08	..	..	24	20.87
5 – 9 yrs.	137	4	2.91	..	..	73	53.28
10 – 14 yrs.	132	8	6.06	4	3.03	83	62.87
15 – 19 yrs.	139	2	1.43	12	8.63	88	63.30
20 – 24 yrs.	57	2	3.50	2	3.50	31	54.38
25 – 49 yrs.	186	5	2.68	11	5.91	110	59.14
50 and over	97	1	1.03	9	9.27	48	49.49
Total	888	29	3.26	38	4.28	460	51.80

A demonstration, including the following undertakings, has been arranged on the Qu'Appelle Indian Health Unit in an endeavour to solve the pre-school problem. (1) Prophylactive vaccination with B C G will be instituted in the hope of protecting the non-resistant group. (2) The Health Unit will gradually be "sanitated" through the efforts of the Medical Superintendent, the Nurse, and the Indian Agents. (3) Such isolation of spreaders as can be accomplished on the reserves and in the unit hospital will be carried out, in an endeavour to reduce massive family infection.

Thirdly, there is the problem of the reserve community as an industrial unit, where the standard of living and the instinct for providence will be gradually improved by the efforts of the Indian Department through their interested agents. Progress in this regard has been very commendable in the past and is a great credit to the Department.

It is considered that this is a program within the economic reach of the Indian Department

even during these years of depression. It will largely eliminate the needless waste occasioned by infection and mortality among children who enter boarding school healthy, and will lay the foundation for a more complete program when economic conditions make this possible.

SUMMARY OF THE FINDINGS OF THE QU'APPELLE INDIAN RESEARCH, 1926-1932

1. In 1931 the Indian tuberculosis death rate for all Canada, omitting the North-West Territories and the Yukon, was 546.73 per 100,000, *i.e.*, 7½ times the tuberculosis death rate for the total population of Canada.

2. In Saskatchewan the Indian tuberculosis death rate in 1931 was 517.42 per 100,000, or 14 times the tuberculosis death rate of the total population of the province for that year. In comparison with the tuberculosis death rate of 646.10 per 100,000 in 1926 the present high figure, however, shows quite a marked reduction.

3. The mortality from tuberculosis among infants up to one year is even higher, the average for this group during the past six years being 1018 per 100,000 for Canada, and 1603 per 100,000 for Saskatchewan.

4. The incidence of active tuberculosis among Indian school children in western Canada is more than 10 times that found among the surrounding white children. These findings have been confirmed by the extensive surveys made by Vrooman and Hill in British Columbia and by Stewart and Meltzer in Manitoba.

5. The general death rate for the Indians of Saskatchewan for 1931 was 17.81 per 1,000, approximately 3 times the general death rate of the total population. The general death rate for the Indians of Canada for 1931 was 17.24, less than twice that for the entire population which was 10.1.

6. In the Qu'Appelle Research area, which is taken as a representative section of the Indian population of Saskatchewan, the disease became epidemic about 1884, reached a height of 9000 per 100,000 in 1890, rapidly fell to 1000 per 100,000 in 1907, and remained between that figure and 800 until 1926.

7. The Qu'Appelle Indian Health Unit, embracing the above research area, was formed in 1930, and the application of anti-tuberculosis measures for the past three years in this unit has been coincident with a further reduction in tuberculosis death rate in this area to 273 per 100,000 in 1931.

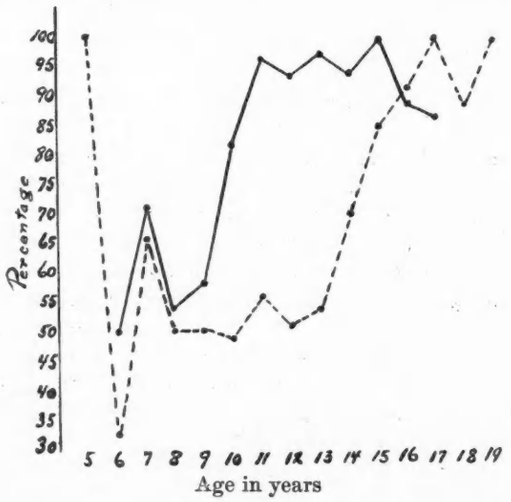
8. Significant changes observed, coincident with the falling death rate in the research area, which may throw light on increasing resistance, are:—

(a) The disappearance of glandular disease. The incidence of glandular tuberculosis was reported by resident physicians attending these reserves as affecting one-third of the population at the height of the epidemic in 1890. Nineteen decimal six per cent of the children in the Qu'Appelle School were operated on for excision of glands in 1906. This malady has receded to less than 1 per cent among the children in the same school in 1932.

(b) A change in the clinical course of the disease. The acute type, terminating fatally in a few months, was the dominant one at the height of the epidemic in 1890. Among 25 cases that have developed in the schools between 1926-32 four, or 16 per cent, were acute, *i.e.*, terminated fatally within a year of the discovery of the lesion. The dominant type of the disease is therefore now chronic, and apart from the non-resistant group referred to above as acute, the more resistant cases show localized disease and appear to be equally as chronic as in the case of our white children of the same age group.

(c) The age incidence of maximum fatal susceptibility is gradually shifting towards that of the surrounding white population. The age incidence of highest mortality was 1-5 years during the first two decades of the epidemic, 10-14 years during the second two decades, and 15-19 years during the period 1927-32. Among the white population of Saskatchewan at the present time the highest incidence of mortality is in the age period 25-29 years.

(d) The age of maximum morbidity in the



Tuberculin sensitiveness in relation to age among Indian school children. Continuous line—*re* 374 children, 1928. Broken line—*re* 273 children, 1933.

reservation population of the research area, which was 10-14 in 1925-26, was approximately the same in the age groups 1-4 years and 10-14 years in the period 1927-32. It will be seen that the high morbidity coincides with the pre-school and school age periods.

(e) No decrease in incidence of morbidity has been observed among those presenting themselves for admission to school. The incidence of active disease found among 657 children on first examination was 7.6 per cent. This incidence is practically the same as that found

among 5504 white family contacts examined in Saskatchewan in 1931-32, which was 7.32 per cent.

(f) In 40 specimens typed, mostly glandular material, the variety of tuberculous infection was found to be human; no bovine infection was discovered. It should be pointed out that the Indians on these reserves have not been drinking milk to any extent.

(g) The incidence of infection in the schools of the Health Unit is considerably lower than previously. The incidence of infection, as indicated by the tuberculin test in 374 children in two schools of an average age of 12.4 years, was 92.24 per cent in 1926-1927. The tuberculin test on 273 children of an average age of 12.35 years in the same schools showed an incidence of 62.63 per cent in May, 1933. The incidence of infection on admission to school was practically the same in 1933 as in 1927, suggesting that home infection is about the same and that the reduction in infection has been due to reduction in school infection. Two possible factors are involved in this reduction, the elimination of bovine infection from the school dairy herds and the reduction of human spreaders in the schools.

(h) Pulmonary lesion cases retained in school, considered closed and non-infectious, as indicated by nutrition, absence of noticeable cough and expectoration, proved to have bacilli in excreta in 11 out of 40 cases investigated, *i.e.*, had positive fæces, urine or both.

(i) Improved living conditions, in the broadest sense, among primitive people are important factors in controlling tuberculosis. This was established on the File Hills Demonstration Colony in the period 1901-1926, where the living conditions approximated those of the white settlers, and it was found that 14 per cent of the third generation of the colony had died of tuberculosis, compared with 21 per cent of the same generation on the adjoining reserve. This fact has been repeatedly observed by officials of the Indian Department on reservations and in schools with varying living conditions.

Medical Economics

THE MEDICAL CARE OF INDIGENTS IN THE PROVINCE OF QUEBEC

BY JAMES STEVENSON, B.A., M.D., F.R.C.S.(C.), F.A.C.S.,

Quebec

It is to my mind quite evident that any discussion on the care of indigents in Canada should commence with the consideration of the situation as it presently exists in the Province of Quebec. Not only was this the earliest settled province in the Dominion, but also it is the province in which the greatest achievement has been accomplished in this difficult problem, and this to the credit of that devoted band of religious workers who since the days of Jeanne Mance and Mère Marie de l'Incarnation have devoted their lives to the relief of the sick and poor. We know that the early colony, through its various vicissitudes, at times suffered severe poverty and distress, and, being as it was far removed from the brilliant court of France and the accompanying evils of feudal tenure in its decadence, it was thrown very much to its own resources. Following the British conquest and the rapid development of the settlements on the seigniorial grants, village life was the predominant feature. The indigent children were adopted by some of the numerous relatives, and the aged who had ceased to be able to carry on the burden of arduous toil were given a nook by the fire-side of some of their numerous progeny. The habitual indigent became a professional beggar, and roamed the country at will, being sure of a welcome at the nearest farmhouse when night overtook him, and what few remained uncared for were taken in charge by some of the many religious institutions supported mainly by private charity.

In such a primitive community, the question of the medical care of indigents was practically non-existent. Doctors were few and far between, and usually unskilled. The sick were nursed to health by wise women who resorted to mediæval methods and remedies whose sole virtue was their nauseousness; fractures and dislocations were treated by the district bonesetter. The growth of industrialism and the development of manufacturing centres, the assimilation of culture from Europe and the United States, the spread of education and decline of illiteracy, have gradually resulted in a change in the nature of the population, from one more or less homogeneous and with no distinctive levels of class, to one in which the classes of wealth, comfortable bourgeoisie, and poverty are more sharply defined. It is with the last class and the care which they are given in times of sickness that we shall deal.

The population of Quebec is now about 3,000,000, of which 51 per cent is rural and 49 per cent urban, and of this latter, over 1,300.000, or 40 per cent, reside in Greater Montreal. Up to within recent years the donations and bequests of charitable individuals and the devotion of the different members of the charitable religious orders sufficed. With the growth of industrialism and the facilities of transportation it has become increasingly easy for the poor to drift to the cities for support and eventually become a

charge on the urban charities. The rural doctor and the rural clergy cannot be entirely exonerated in "passing the buck" to the cities. The charitable institutions, with true Quebec spirit, finding themselves in difficulties, appealed to the local and Provincial Government for financial help. The Government, looking for a source of income to meet the demands which no political party dared refuse, turned to taxation, and the Quebec Public Charities Act, or Loi de l'Assistance Publique, was the outcome. The Provincial Government, with a rather Gilbertian sense of humour, determined that the population of the Province of Quebec would prefer to raise the extra cash for this purpose by a tax on pleasures and that such a tax would be the least objectionable and easiest to collect.

The Quebec Public Charities Act therefore exacts that each municipality should expect to pay the cost of the care of its indigents, whether treated in that municipality or not. A fund known as the Municipal Charities Fund should be formed in each municipality to which goes one-half of the money collected from the municipal amusement tax, the other half of the money collected being turned over to the Provincial Government to form the basis of the Quebec Public Charities Fund. This fund is further supplemented by the percentage collected from race-track meets, the tax on all meals in restaurants, a percentage of the price of admission to all theatres, halls and other places of amusement, and part of the profit, if any, of the Quebec Liquor Commission, not to exceed $1,000,000 per annum.

The scope of the Public Charities Act is very wide, as may be shown from the report of the Director of Public Charities for the year 1932. There are 207 recognized institutions, classified as follows:— (1) general hospitals; (2) sanatoria and tuberculosis hospitals; (3) homes for old people, epileptics, and paralytics; (4) orphanages; (5) foundling and maternity hospitals, and other charitable organizations not otherwise classed; (6) institutions for crippled children. These receive from the Fund an amount per diem per inmate of two-thirds the estimated cost of maintenance, which allowance runs from 24 cents per day in orphanages, to $2.00 per day in general hospitals and sanatoria of over 40 beds. The lowest amount paid to an institution for the treatment given to indigents for the year 1932 was $2.72, and the highest $177,229,92. The contribution from the various municipalities likewise showed an even wider variation, from 90 cents to $771,136.28, with a grand total of $1,301,045.09. The total collected for 1932 from all sources was $4,322,-022.09. The amount expended by the Bureau of Public Charities has grown from $327,665.61 in 1922 to $4,764,124.34 in 1932.

What is an indigent? Every applicant for charity considers himself an indigent. The law, however, through the Public Charities Act, requires that proof of indigence must be submitted as follows:—

1. An application on a special form signed by himself, a relative, friend or tutor.
2. A sworn certificate from the municipal authorities where the indigent belongs, to the effect that the applicant is an indigent, after they have satisfied themselves that neither the applicant nor those of his relatives who are obliged by law to support him are able to pay for his support in the institution to which admittance is asked. If these requirements can be met, the applicant is then admitted and paid for from the Fund.

The above summary of the workings of the Quebec Public Charities Act is all very interesting, and shows what has been done by systematic state assistance to organized charities for the care of indigents; but, and this is the question that interests and affects the medical profession, no provision is made to recompense the doctors for the services which they give to these indigents, and while they are taxed equally with the rest of the population to support the institutions, they are in addition expected to give their services to these institutions free. This is a poor principle and unjust to the profession. If the indigent is the ward of the state to the extent of two-thirds of his cost of maintenance, should not an allowance be made to cover at least half the cost of medical attendance, as is done by the Federal Government in the case of Indians and sick mariners? The Provincial Government has always hesitated to include this item in their law, no doubt fearing that this would open the door to exploitation of the Fund by many members of the profession, and they probably have in mind the experience of the Quebec Workmen's Compensation Commission in their difficulties in formulating and applying a medical tariff to industrial accident cases, who, when all is said and done, might be classed as potential indigents, were it not for their protection under the Workmen's Compensation Act. It is interesting to note that in 1932 the Quebec Workmen's Compensation Commission expenses for medical and hospital care of 37,115 injured workmen amounted to $567,-921.59, for an annual payroll of about $170,-000,000 for about 200,000 employees, not including the amount expended by the employers in schedule 2. (Railways, Government and Public Utilities).

RURAL DISTRICTS

In sparsely settled and poor rural districts, and unorganized territories such as the lower Saguenay and North Shore where the population cannot support a licensed practitioner, the Provincial Bureau of Health will occasionally subsidize a doctor, or place a resident trained nurse, or even maintain a small hospital to look after the medical needs of the district. The main objections in this case are (1) the difficulty

of finding competent doctors willing to practise under these unfavourable conditions; and (2) the tendency on the part of the resident district nurses to undertake work outside their province and for which they have no training or qualifications, which might bring them into conflict with the Provincial Licensing Board.

COUNTY HEALTH UNITS

Let us now consider the work which has been done by the Provincial Bureau of Health through the establishment of these units. The principal objective of the unit is that of protective medicine. Each Unit consists of a Health Officer, assisted by nurses, a sanitary inspector, and a secretary whose work consists of epidemiology, the collection of vital statistics, pre-school clinics, sanitary and school inspection, maternity advice, and general educational work. The cost is from $11,000 to $14,000 per Unit per annum, shared by the county, the province, and the Rockefeller Foundation. This work in Quebec dates from the Quebec Health Units Act of 1925, and was inaugurated in 1926. There are now in operation 28 units, covering 36 counties, and serving a population of 900,000 people. In addition to the public health and sanitary inspection activities, the most important work which they have done is in connection with the travelling clinics for tuberculosis. During the year 1932, 23,893 persons were examined at 1,046 stationary or travelling clinics, and of these 2,183 were diagnosed as suffering from active tuberculosis.

These Health Units are not, as elsewhere, purely local and autonomous, responsible to the county authorities only, but are an integral part of the General Health System of the Provincial Health Service, and the direction comes directly from this central office. Appointed and paid from this, the personnel reports every week to the central authority on all work done. To quote Dr. Lessard in a recent address. "We have thought that in our Province at least, and as far as Public Health and its administration are concerned, direction, command and orders must come from a governing body, and our population is astonishingly willing to comply with such a system. More than that, in several counties we have many small towns and cities with a population of 6, 8, 10, or 15 thousand people which were provided before with a small part-time health service; we have taken in our hands the care of their public health. . . and the municipal authorities of these towns are so satisfied with the efficiency of the system and are so glad to be free of the patronage evil, that they tell us, all of them, they would never consent to go back to their old régime."

What is the future program of the Bureau of Health? To quote again from the same address:— "We shall not interrupt our effort until the entire Province, so far as the rural and semi-rural population are concerned shall have been covered by the Health Unit system. There is a possibility of 50 or 55 Units in our territory, and I am convinced that before another five years have elapsed, our program will be accomplished and our aim attained."

All this work has not been accomplished without criticism, and much has been written in the local medical press against the system. On the other hand, there is no denying that results have been obtained which fully justify the stand taken by Dr. Lessard and the continuance of their functioning. It is also obvious that if such service works to a more satisfactory degree to better the health and general welfare of the population than the spasmodic and often ill-directed efforts of the country practitioner in the past, so much the worse for him, as progress must be maintained.

VENEREAL DISEASES

In 1932, in Quebec, there were 80 centres of treatment, with approximately 175 physicians. In addition to the Quebec and Montreal laboratories, reports are made in the General Hospitals of Quebec and Montreal. In these dispensaries or centres of treatment 294,782 treatments were given in 1931. In connection with the cost of this, a considerable deficit had been foreseen, which has unfortunately materialized, and unless aid is obtained from the Provincial and Federal Governments it will be impossible to continue the free distribution of drugs required for the treatment of venereal diseases.

INSTITUTIONAL ACTIVITIES

Having discussed the various forms of governmental activities, I shall now consider briefly the activities of the institutions themselves. In Quebec, as elsewhere, practically all these have amongst their personnel one or more doctors to supervise or give the necessary medical care to the inmates. These doctors may be, on the one hand, on full or part-time salary, or, as in most cases, may give their services free. In the case of those on salary, it is obvious that a proportion of this is paid indirectly from the Public Charities Fund by means of the per capita per diem allowance. Therefore the greater the number of salaried physicians, the higher will be the cost per patient. This no doubt, is one reason why the large general hospitals are continuously complaining that the allowance of two dollars per day does not cover the hospital costs. In these hospitals and public clinics the public patients are usually treated without any extra charge by the attending staff, though in some of them, the staff are allowed to collect a small fee according to the patient's means, over and above the regular hospital charge. In the case of indigents this is, of course, impossible, and while the institution is paid two-thirds of the cost of maintenance, the attending staff receive nothing for their services but the questionable gratitude of their patients and the experience,

which is, in the case of senior men, often superfluous.

What are the objections to this system? (1) Exploitation of the public wards and free clinics by patients who are able to pay at least a small fee for the medical treatment. (2) A tendency for large hospitals to go into the practice of medicine, by accepting a fixed charge per diem to include all medical and surgical care and obliging their attending staff to give these without fee or recompense other than the privilege of practising in the hospital. It was to correct this that the Quebec Workmen's Compensation Commission insists that all medical and surgical accounts against them should be made out in the name of the doctor rendering the service. (3) The attitude of the Provincial authorities in leaving the doctors entirely out of the picture in drafting the law and assuming that the institutions will see that the poor and needy are given the necessary care without charge. As long as the indigent is dependent of private charity, no one of us will quarrel with the principle of giving our services free. It is, however, decidedly unfair to the profession whenever the indigent is recognized wholly or partially as a ward of the state. Even the Courts of Justice allow the costs of an advocate appointed by the Court to defend a person who is unable to pay for his own defense.

What are the prospects for the future? To quote from page 47 of the 2nd report of the Quebec Social Insurance Commission:— "In Hospitals, the control of the Religious Orders, *aided by a picked staff, working almost without salary,* results in the saving of at least a dollar a day per bed. A Christian society owes it to itself to maintain good works of all sorts, but it is in the general interest that the burden borne by the productive part of the population be not too great and it is in the interest of the poor themselves that their upkeep be not too expensive." (The italics are mine).

This attitude, aided, no doubt, by absence of organization on the part of the profession is, in part, responsible for the lack of consideration to the doctors in the existing schemes of indigent relief and corresponds closely with the attitude of the authorities in their recent decision not to consider medical care to unemployed families as "Direct Relief."

The Quebec Social Insurance Commission, notwithstanding that they have submitted a very complete report on the various phases of the problem, are very hesitant in recommending any very definite scheme, and as regards Sick and Disability Insurance, which is the matter which most concerns our profession, their recommendation is as follows:—

"Having considered the different aspects of the question, the Commission believes that it is advisable to attempt a partial solution by suggesting that here as in Europe the system may be adopted gradually. It is the opinion of the Commission that recourse should be had to the subsidized optional régime before the obligatory system, all the more because the subsidized optional régime will be easy to apply, since Mutual Benefit Assurance societies already exist and it would be sufficient to make use of them. . . The Commission is of the opinion that a law should be passed. . . with a view to authorizing the formation of such societies as The National Society of Hospital Treatment, which would accept contributions from employers and workers and receive a grant from the state, the amount to be determined according to the character of the society, *i.e.*, country or urban. The Mutual Societies already in existence might institute a service including only payments in kind while continuing money payments to members who wished to receive them. . . . This régime which could be developed by careful publicity would little by little accustom the people to the idea of sickness insurance; it would ease the burden on public charity and have valuable results on general health. In all these cases it would constitute an experiment which without any doubt should be attempted, a minimum trial the results of which could be carefully studied. As a result of this experience the public authorities will be able to decide, after an interval of five years, whether it is advisable to institute obligatory insurance, taking into consideration at the same time the principles and data which we have attempted to assemble in this report."

There is no question to my mind, but that were it not for the depression, legislation along the lines recommended by the Social Insurance Commission would have been brought forward in the Provincial House this coming session.

In this report, as in the Quebec Public Charities Act, no reference is made to the part to be played by the medical profession, and we are led to infer that in the future as in the past we will be expected to care for the mass of the people, for these are the ones to be protected by the proposed legislation, without the hope of any earthly recompense. Virtue may be its own reward, and a crown in Heaven a laudable aim, but to the average practitioner five shillings goes farther on earth towards feeding and educating his family. I feel that the self-respect of the population in general and the profession in particular would be better maintained if the false principle of "something for nothing" were discarded. Surely the labourer is worthy of his hire.

In writing this article I had not intended to encroach upon the contentious question of State Medicine but I find it very difficult to refrain. After reading in the various reports that 900,000 persons are already served by the Health Units and service to at least 1,500,000 is contemplated in the near future; that about 300,000 are covered so far as occupational accidents are concerned by the Workmen's Compensation Act; the recommendations of The Social Insurance Commission that all employers be held responsible for the health and medical care of their employees, it would not require much imagination to prophesy that some form of partially subsidized State Medicine under the direction of a Government bureau is closer than most of us imagine.

SUMMARY AND CONCLUSION

I have described briefly the system of caring for indigents in the Province of Quebec, and have endeavoured to call attention to some of the deficiencies from a doctor's point of view. I have not attempted to voice all the criticisms against all the various parties interested, nor have I touched on the attitude taken by the different medical bodies, provincial or local. I hope that what I have said will be taken impersonally and without offense, and that by opening the discussion I will be followed by others, not excepting the Director of Public Charities himself, for whom I have the greatest regard, and thus by a free and dispassionate discussion of the problem, justice and fair treatment may be obtained for us in coming legislation.

State Medicine as part of the scheme of Social Insurance is coming very soon in Quebec, and it behoves every medical man to give the matter careful thought, and when the time comes for him to be ready to back up and support those whose task it will be to represent the medical profession. I would say, and I don't want this to be taken personally, that were the demands of the profession presented in as orderly and organized manner, as was done by the representatives of labour, these demands would not have been passed over in such a cavalier manner. I know that I am accusing my profession of supineness, or at least lack of cohesion and organization, and I would gladly see future events prove me wrong.

REFERENCES

1. Reports of The Quebec Social Insurance Commission.
2. Report of Quebec Workmen's Compensation Commission, 1932.
3. Report of Director of Public Charities, 1932.
4. Report of Quebec Public Health Service, 1932.
5. Report of Executive Committee, Canad. M. Ass., 1933.
6. Quebec Public Charities Act.
7. Quebec County Health Units Act, 1925, and 1933.
8. Address by Dr. A. Lessard, Director Quebec Public Health Service, before American Public Health Assoc., 1931.
9. Mémoire Lesage-Bazin, from Pro. Que. Med. Assoc. to the Social Insurance Commission.
10. WOLFENDEN, H. H., The Real Meaning of Social Insurance, Macmillan, Toronto, 1932.

THE MEDICAL ECONOMIC SITUATION IN NEW BRUNSWICK

BY C. J. VENIOT, M.D.,

Bathurst, N.B.

The medical economic situation in New Brunswick can be summarized in a very few paragraphs, as it covers little more than the fluctuations of professional incomes experienced during the past five or six years. In New Brunswick, so far, there has not been a suggestion of State Medicine or of Social Insurance. No mention of them has been made by the provincial government, the municipalities, or by labour and other organizations. On these scores the medical mind is at rest. What the future holds in store in this direction still remains in the lap of the gods.

The activities of the Provincial Department of Health deal with the prevention of disease along the lines adopted in other provinces. Vaccination against small-pox and inoculation against diphtheria are carried on extensively by district medical health officers.

Industrial accident cases are taken care of by the Workmen's Compensation Board, as in other provinces, with a fair schedule of fees arranged by mutual agreement between the New Brunswick Medical Society and the Compensation Board.

Some of our industries, through group insurance, protect their employees against illness other than industrial accident cases, providing hospital care and indemnity for loss of time, but no remuneration for medical services.

Professional incomes reached their peak from 1923 to 1929, during which time the average collections attained about 65 per cent of services rendered. Since the advent of the depression period incomes have been steadily on the wane, and have dropped in many districts to less than one-third of what they were five years ago. In several districts at the present time physicians are barely collecting enough to pay living expenses. Practitioners in the rural districts seem to suffer most from the present depression. The curtailment in the lumber and pulp industries, which a few years ago formed the backbone of the province's wealth, together with the lack of market for farm products, has had a natural reflection on professional incomes.

In New Brunswick nothing has been done to remunerate professional men for services rendered to patients who come under direct relief. Some municipalities, those who supply medical care to their ordinary indigents through their Alms House Commission, included some of their unemployed sick in this class, but this favour covers only a minimum part of the medical services rendered to persons on the unemployed list and to members of their families.

In conclusion, the financial position of the medical profession in general in New Brunswick, while not desperate, as in some of the western provinces, certainly leaves a lot to be desired.

What remedy can be applied to the present situation? Practically none, excepting to await patiently a favourable turn in the business tide. Subsequently to the interview which a special committee of the Canadian Medical Association had with Premier Bennett concerning the inclusion of medical services to the unemployed as part of direct relief, members of the medical profession received an intimation that the finances of the province were not in a position to permit the desired inclusion of medical services as a direct relief measure. No further action has been taken by the profession along these lines.

THE WINNIPEG PLAN

The greater number of municipalities which constitute Greater Winnipeg have accepted the Winnipeg plan of payment for medical services rendered to those on relief. Very recently St. Boniface came into line with Winnipeg. The special relief committee has arranged that the largest amount that can be drawn by any one practitioner from Winnipeg and the other municipalities adjacent is a total of $100 per month. The committee has also decided that 5 per cent will be deducted from accounts paid by the city to doctors under this scheme, and that 5 per cent will be paid to the trustees of the Winnipeg Medical Society and will constitute a fund to defray expenses in connection with administration. It is not too much to say that the success obtained by the doctors of greater Winnipeg is in large measure due to the ability of Dr. E. S. Moorhead, Chairman of the Special Relief Committee, and of Dr. A. J. Swan, the Secretary.

ROSS MITCHELL

Notes on the British Pharmacopœia and Canadian Formulary

Calamine

Calamine is a zinc ore which is found abundantly in Germany and England, and to some extent in the United States. The colour varies from pure white to brownish or green or blue, and is attributed to various impurities, such as iron and manganese. The name "calamine" was applied indiscriminately to zinc carbonate and hydrous zinc silicate, owing to the close resemblance of the two substances. Identification can be made only by chemical analysis. As early as 1803, James Smithson showed by analysis that naturally occurring pure zinc carbonate contained 35.2 per cent of carbon dioxide and 64.8 per cent of zinc oxide. In 1832 F. S. Beudant restricted the name "calamine" to zinc silicate and in honour of Smithson named the carbonate smithsonite. Dana and many other minerologists still use this terminology. In England, Brooke and Miller designated zinc carbonate as "calamine", and the silicate as "smithsonite", and this reversing of the terminology has led to considerable confusion. The carbonate is known also as zinc-spar and the silicate as hemimorphite; the silicate is also called electric calamine.

Some authors maintain that much of the calamine on the British and American markets about 1850 was a spurious mixture containing sulphate of baryta 78-87.5 per cent, the remainder being oxide of iron, carbonate of lime, sulphate of lead with traces of zinc. Miners distinguished between brass calamine, which was sold to manufacturers of brass, and baryta calamine, which was often supplied to pharmacists. As a result of many investigations a great improvement took place in medicinal calamine.

The "calamine" employed in pharmacy (calamina, lapis calaminaris) originally referred to native zinc carbonate. When of good quality, it was almost completely soluble in dilute mineral acids, emitting bubbles of carbon dioxide. When soluble in sulphuric acid it contained but little carbonate of lime and no barium sulphate. The native carbonate, however, contained such impurities as iron and silica, and as the calamine of pharmacy must be impalpable, it was difficult to obtain such a preparation from the impure native product by pulverizing with apparatus such as existed in the earlier days. As a result, the native calamine was roasted, during which process some of the carbonate was decomposed to oxide (the amount depended on the particular temperature employed). The resulting product was more easily powdered, but since it was no longer native calamine, it was called prepared calamine. This product contained so many impurities, that in 1850 it was omitted from the United States Pharmacopœia and in its place was substituted Zinci Carbonas Præcipitatus. The British Pharmaceutical Codex, 1907, provides for two calamine preparations, one, the prepared calamine which is made from native zinc carbonate calcined at a moderate temperature and is freed from gritty particles by elutriation; it must be almost entirely soluble in mineral acids with some effervescence. The other preparation, artificial calamine (calamina factitia), is made by treating zinc sulphate and ferric chloride with sodium carbonate; the resulting precipitate is calcined until no effervescence occurs when treated with acids.

The National Formulary, 1926, states that prepared calamine contains not less than 98 per cent zinc oxide, with some ferric oxide and silica as an impurity. The United States Pharmacopœia X includes precipitated zinc carbonate and zinc oxide, whereas the British Pharmacopœia 1932 includes only zinc oxide.

The Editors of the Canadian Formulary, when preparing a monograph for calamine, considered the chemistry of calamine from its various angles. It appeared that the calamine commonly used in pharmacy consisted mainly of zinc oxide, for in the calcining of the native carbonate decomposition must occur. Further actual tests of the calamines on the market showed that they contained about 98 per cent of zinc oxide. In view of the fact that the solubility of zinc oxide and zinc carbonate is the same, 1:100,000 at 15°C., it would seem that it mattered but little whether the prepared calamine contained the

oxide or carbonate. With newer methods of powdering native calamine, no doubt excellent preparations can be prepared, but the decision as to whether these are of greater value than the Canadian Formulary preparation or zinc oxide, must be left to the clinician, for chemically, on the basis of solubility, no difference should exist.

The Ephedrine Sprays, C.F.

The Canadian Formulary includes two ephedrine nebulæ. On account of its greater stability and prolonged action ephedrine has replaced adrenaline in nebulæ and is usually employed in 1 per cent solution of the free alkaloid in liquid paraffin. The compound nebulæ contain singly or in combinations such substances as menthol, camphor, thymol and eucalyptol. Recently, aqueous solutions of ephedrine, chlorbutanol, eucalyptol and phenol have appeared on the market, but as yet have not supplanted the oil nebulæ.

A 1 per cent solution of ephedrine in liquid paraffin produces a good vasoconstrictor effect, causing some burning and temporary discomfort. Children readily tolerate a ½ per cent solution, which seems to be efficient for them. When the other drugs mentioned above are included with the ephedrine the nasal passages are cleared more rapidly, but there is frequently more temporary discomfort.

As the hydrochloride of ephedrine is not soluble in oils, the free alkaloid must be dispensed when oil is prescribed. In order to facilitate the solution of the ephedrine in the liquid paraffin, it is first dissolved in oleic acid in quantities as indicated in the Nebula Ephedrinæ C.F. and Nebula Ephedrinæ Composita C.F. When the nebulæ are being used as nasal drops the greatest efficiency is gained by administering them as indicated by Henderson, Beach and Johnston (*Canad. M. Ass. J.*, 1931, **24**: 684).

V.E.H. AND G.H.W.L.

Men and Books

SIR WILLIAM OSLER—PARASITOLOGIST

BY THOMAS W. M. CAMERON,

Professor of Parasitology, McGill University, Montreal

Sir William Osler is so well known as a clinician that his many important papers on the entozoa of man and animals are often overlooked. His most active period as a parasitologist was early in his career. At this stage his inclinations were undoubtedly leaning in the direction of that science which has since made such enormous developments, especially in the tropics, as an ancillary branch of medicine. He continued to study medicine rather than biology, however, and in gaining a great physician, the world lost a great naturalist. Under the stimulating influence of his old head master, the Rev. W. A. Johnson, an omnivorous amateur naturalist, young Osler developed that interest in biology and parasitology which never left him. He went to Trinity College in 1867, and in February of the year following he commenced his collection of entozoa.

Trichinosis.—In the winter of 1870, he drew attention to the presence of cysts of Trichina in the muscles of one of the bodies in the dissection room. (He had, however, already studied this worm under the microscope, as he states in his note-book.) Innumerable sections were cut and feeding experiments undertaken, because the disease was then little known in America. Six years were to elapse, however, before he published his first paper on the subject.

> "When a student with Prof. Bovell of Toronto I had several opportunities of studying these parasites. In the month of February, 1870, while dissecting a subject with Dr. Zimmerman in the Toronto School of Medicine, we discovered numerous trichinæ throughout the whole muscular system, all of which were densely encysted, many having become calcified. From a single drachm of one of the muscles of the arm I obtained 159 cysts, the greater number of which enclosed healthy looking worms. This man was a German, and had been janitor at the Hospital, where I had known him for over two years."

He returned again and again to this most important subject. In 1883, he stated that from 1000 hogs from western Canada, selected at random, he had found only 4 infected with *Trichinella spiralis*, while he had only records of sixteen human cases in the country—three in Hamilton (1868) with two deaths, nine in Montreal (1869) and four cases he himself had discovered during 900 autopsies. One of these had been used successfully to infect a rabbit. In 1899 he had had personal experiences with eleven human cases, and he quoted Flexner to the effect that three cases had been seen in 1000 post-mortem examinations at Johns Hopkins. He discussed his own clinical cases at length, commenting on the well-known symptoms of muscular pains and swelling and pointed out for the first time the great diagnostic importance of the enormous eosinophilia which so frequently accompanied the disease. Trichinosis is still a sporadic disease in pork-eating countries and it is far from infrequent in the North American Continent. It is not sufficiently frequent, however, to be easily recognized by every physician, and most cases are diagnosed as enteric fever until Osler's tell-tale eosinophilia reveals their true nature. His

investigations into the incidence of Trichinosis in the pork supply of Montreal, led him to study two other important parasites transmissible to man, in both of which the pig was intimately concerned. The first of these was hydatid disease, the second, cysticercosis.

Hydatid.—He found the multiple cysts of this dog tapeworm in 31 out of 1037 local pigs during this survey, but he had knowledge of only eight to ten human cases in Canada. He was never able to record a natural infection of echinococcus in the dog in Canada, although in 1885 he fed cysts to a dog and recovered the adult worms seven weeks later. In the previous year he recorded the case of an Ontario man of 58 who passed ten to twelve daughter cysts, (many containing grand-daughter cysts) with the urine, and commented on the rarity of the condition. At that date he was able to find records of only 61 other human cases in North America. Within a year, however, he was able to add 6 new cases to these records. In 1880 he recorded the same parasite from the liver of a tramp, recalling that, although it was uncommon in Canada, he had records of cases both from Montreal and the Eastern Townships.

Cysticercosis.—Man, in North America, is parasitised by two species of tænia, both of which are transmitted to him through eating under-cooked meat—in one case pork, in the other beef—and Osler studied both. In his survey of Montreal pork he found that *Cysticercus cellulosæ* was common, 76 cases of liver infection being observed in 1037 pigs. Only the livers were examined, however, and the proportion accordingly was probably too small. At that time, he estimated that there were 200 cases of human infections in Montreal with adult tapeworms.

In the previous year (1892), Osler, with his student, A. Clement, of the Veterinary College, had fed a three days' old calf with fifty ripe segments of *Tænia saginata* from man, and seven weeks later he found that the muscles were heavily infected with *Cysticercus bovis,* although no obvious symptoms had been noted during the interval. He commented on the practical difficulty in seeing the cysts, and believed that lightly infected beef must often be overlooked by the meat inspector.

In 1885, he recorded a very heavy infection with the pig cysticercus,—his material came from Berlin, however,—and he demonstrated how the cysts in such a case could be seen on the tongue during life. In 1891, he found a case of human infection with the same parasite, in a German, 43 years of age, who had resided in the United States for five years. He was able to count no fewer than 74 cysts: but there were no symptoms of infection of the central nervous system, and the patient made an uneventful recovery.

Filaria bancrofti.—His other researches in human helminthology included a demonstration (1890) of living embryos of *Filaria bancrofti* from a man who had harboured the parasite for eighteen years. He was able, by surrounding the coverslip with paraffin, to keep them alive for nine days. He also recorded a very heavy infection with oxyurids in a patient of twenty-five years, who had been infected for two and a half years; the parasites were finally expelled by the use of quassia enemata.

Osler's interests were by no means confined to human helminthology, however, and he early recognized the value of comparative study. He was, in fact, one of the first sponsors of that youngest branch of medicine which we now call comparative medicine. He visited veterinary hospitals and abattoirs; he taught in the Veterinary College at Montreal, (in his papers he calls himself Professor of Physiology of the Veterinary College, Montreal; Lecturer in Helminthology, Montreal Veterinary College and Vice-President of the Montreal Veterinary Medical Association,) and he wrote a number of papers dealing with purely veterinary parasitology. He was a true comparative parasitologist, however, and studied entozoa from almost any source, as his note-books show.

"'21/iv/70. On the fins of chub in the Rev. W. A. Johnson's aquarium were noticed several round white spots. These on examination proved to be some sort of entozoa. In addition to these, some yellow spots were seen which seem to be a more advanced condition of the parasite. (See slide . . .).'

"Another entry the following days records the catching of a pike 2 ft. 7 in. long, from which he obtained '68 specimens of tænia and two or three small Ascaridæ,' the microscopical characteristics of which he proceeds to describe in detail.

"On other days he shoots a hawk, or hooks a large black bass in Burlington Bay, or examines ten sunfish caught in the canal, and so on—a combination of sport and science, with the chief emphasis on science, to judge from the elaborate notes on his pathological findings and the scant reference to their source.

"Specimens were obtained from many sources, as his notes indicated—from the Montreal Fish-market, from the Natural History Society through whom he secures a dead lynx for study. '8/3/371. From a rat at Montreal General Hospital I obtained 5 tæniæ from low down in intestine—a small fine species with motor-vascular system very distinct,' etc., etc."

This was very probably *Hymenolepis diminuta.*

One parasite from the gills of a newt was handed to Professor R. Ramsay Wright for description and in Wright's first paper from Toronto it appears under the name of *Sphyranura osleri,* nov. gen. et sp.

"I have lately received," he wrote, "from my friend Professor Osler, of Montreal, several specimens of a worm taken from the gills and cavity of the mouth of our common lake-lizard (*Necturus lateralis,* Raf.). These had been preserved for eight years in Goadby's fluid, and proved to be comparatively useless for further examination, having become quite opaque and black in colour. From some specimens, in a good state of preser-

vation, mounted by Dr. Osler for microscopical examination, and also from his notes and sketches made on observation of the fresh specimen, I am able to communicate the following.''

In the more strictly veterinary field, in addition to the parasites mentioned above, he made a number of noteworthy contributions. In 1877, he investigated, at the request of Principal McEachran of the Veterinary College, a pneumonic disease which had broken out among the pups of the Montreal Hunt Club. A number of fatal cases were reported and on autopsy he found numerous small parasitic worms in the trachea and bronchial tubes. In his paper he described 8 cases in detail and recognizing the worm as new, he called it *Strongylus canis bronchialis*, a name subsequently changed by Cobbold in 1879 to *Filaria osleri*. In 1921, Hall erected a new genus for it and its name is now *Oslerus osleri*. It has since been found in many animals and many countries, but in spite of the researches of Hall, Vogel, and the present writer, our knowledge of it is still scanty and incomplete. In the same dogs he found Dipylidium, ascarids, hookworms and whipworms. He also discussed lungworm disease in general, and stated that he could find no records of its occurrence in Canada.

In 1882 he exhibited specimens of *Amphistoma conicum (Paramphistomum cervi)* from Pictou County, Nova Scotia, mentioning that they were very common in that district. And in 1884 he exhibited specimens of liver fluke disease in sheep. He stated that while in Berlin, he spent two afternoons weekly at the abattoir there, collecting parasitic and other material. The liver which he exhibited was affected with a chronic cholangitis and not greatly cirrhotic, but he pointed out that ''rot'' in its advanced stages closely resembles human cirrhosis.

His most important economic investigation, however, was that in which he described the parasites of the Montreal pig supply, referred to above.

> ''This timely investigation was of great public service and was a contribution to the health and hygiene of the community which probably had more weight as coming from a physician holding no political office, than had it originated from some other source.''

His studies on protozoology also began early in life, and in 1883 he published his first paper ''On Certain Parasites of the Blood of the Frog,'' which began as follows:

> ''In my Practical Histology class, during the winter of 1881-2, while the students were working at the blood of the frog (*Rana mugiens*), I noticed in one of the slides a remarkable body like a flagellate infusorian. I thought that it was one which had got into the blood, at the time of withdrawal, from the water on the web of the foot. Meeting with examples in the slides of several other students, my attention was again directed to it and I made several sketches and wrote down the following description....''

> ''The parasites proved to be varieties of *Trypanosoma sanguinis*, and though the observation, as he found, was not original, for Ray Lankester had previously described them, he gave an account of the behaviour of these bodies within the blood cells in a way which indicates his alert powers of observation.''

> ''On March 22nd of 1890, he discovered amœbæ in the material secured from an abscess of the liver of a patient with chronic dysentery whom he had seen in consultation with Dr. Friedenwald, of Baltimore, and on whom Dr. Tiffany had operated. In one of his case note-books which has been preserved, he had drawn numerous pictures of the organism, especially of one amœba which on March 24th was watched for many hours, and of which there is a succession of sketches showing its changes in contour. Two days later he wrote enthusiastically to Musser:

> 'We have been much excited over Kartulis' amœbæ, which we have found in a liver abscess from a case of dysentery—a Dr. from Panama. They are most extraordinary and striking creatures and it takes one's breath away at first to see these big amœbæ—10 to 12 times the size of a leucocyte—crawling about in the pus. The movements are very active and in one case kept up for ten hours. . . . Koch and Kartulis found them constantly in the stools and bases of the ulcers in Egyptian dysentery and the latter in the liver abscesses. Keep an eye on your Blockley dysenteries as it would be most interesting to find similar bodies in our dysenteries.'

> ''An account of this observation was promptly written up and appeared in an early number of the 'Bulletin'. It was the first confirmation in English-speaking countries of observations made by an Athenian, Kartulis, who had been stimulated to make studies of dysentery in Greece, following upon the discovery by Koch during his sojourn in Egypt in 1883 with the Cholera Commission, that amœbæ were occasionally to be found in the intestines of persons dead of dysentery. Up to this time a good deal of doubt had been cast upon the conclusions of Kartulis, for many had regarded the amœbæ as secondary invaders, so that the discovery of the parasites in the liver abscess Osler regarded as the first important observation made on the medical service. Late in 1913, when preparing for the address....in which he gave a summary of his life as a clinical teacher, he wrote certain sections not included in the article when printed. One of them refers to this discovery and its sequel, as follows:

> ''Familiar with the various forms of amœbæ, the opportunity appeared to be an important one for the study of a disease which was widely prevalent. We very soon had other opportunities, and within a few weeks Dr. Lafleur demonstrated their presence in a local case. In the same year the amœbæ were demonstrated by Dr. Charles Simon in a case in the wards, in which the abscess had perforated the lung. The disease was found to be common, and Dr. Councilman in the Pathological Department, and Dr. Lafleur, then first Assistant in the Medical Clinique—issued in Vol. II. of the Johns Hopkins Hospital Reports for 1890 the monograph on the subject which still remains the most exhaustive contribution in English, and at once convinced both pathologists and clinicians of the specific nature of this type of the disease. Many subsequent reports are to be found scattered through the Bulletins, one of the most interesting of which was the disclosure by Dr. Flexner of the presence of the amœbæ in an abscess of the jaw. The hepatopulmonary abscess—of which we had a great many cases—was made the subject of a careful study by Dr. Futcher'.''

In April of 1886 he saw—and drew—the amœboid stage of the malarial parasite, but he was not convinced of the fact that the parasite was really a causal organism and not an effect,

until autumn, and in 1887 he published his paper on the Hæmatozoa of Malaria, in which he placed himself amongst the foremost of the investigators on this subject. Thereafter, however, he devoted himself mainly to the diferential diagnosis of the most widespread of all human diseases, from other obscure febrile conditions. He had the power—as also had that other great worker on medical parasitology, Patrick Manson—of infecting others with his enthusiasm, and much valuable work was carried out by his colleagues and students.

Malaria is still captain of the forces of death, but it is now only a question of time before it is finally conquered. To the roll of honour of the great pioneers of the subject—Manson and Ross, Laveran and the others, must be added the name of Osler.

An immense amount of time was spent in the study of seventy cases of malaria. Hourly examinations of blood were made and he observed the formation of the rosette forms during paroxysms of malarial fever. He had a previous knowledge of blood protozoa, as his own observations on frogs show, and he was well acquainted with the work on Surra carried out in India by Evans (who was also a McGill medical graduate). He believed that the flagellate forms were the adult stages, but final proof of this had to await the completion of MacCallum's studies on bird malaria. He was enthusiastic in his advocacy of the microscope as a diagnostic agent, and expressed his conviction that blood examination would prove a most valuable aid in the elucidation of obscure cases in malarial regions; in fact, he later insisted that no diagnosis should be made without the demonstration of the parasite. He also carried out pioneer work in the differentiation of the three different species of malarial parasites.

Much of Osler's work in the wide field of parasitology has been lost, but there remains enough to stamp him one of the great pioneers in medical zoology. Even when pressure of work prevented him continuing his own field and laboratory work on the entozoa, he still retained his interest and his enthusiasm as is shown by the following letter to Professor J. W. Robertson, Montreal.

"When in Montreal a few weeks ago, I had a chat with Sir William (Macdonald) and Mr. Peterson on the possibility of organizing, in connection with the Agricultural College, an extensive Department of Medical Zoology, in which the whole subject of parasitism should be considered. Sir William was anxious that I should see you, but I had only part of two days in Montreal. I promised him to get a scheme from Stiles of Washington, who is certainly the leading expert on parasites in the English-speaking world. The department could be made a most important one and it has such close affiliations with disease that the same man could very well lecture on parasites in the medical school. There would be no lack of candidates for such a place, and there are one or two very good men available, particularly Todd who has done so much good work on the ticks. I should not be surprised, however, if such a position were thrown open, that Stiles himself might be a candidate. I have asked him to prepare a memorandum which I will forward to you."

Professor Stiles drafted the memorandum, but it has now been lost. He was unable to consider coming to Canada, however, as his personal interests were all in the South and he did not wish to leave the southern climate in which he had laboured so thoroughly and effectively. In that year, however, Dr. Todd was appointed Associate Professor of Parasitology at McGill, and a beginning was made with Osler's scheme. Twenty-five years of crowded progress in the science he loved were to elapse however before his vision was fulfilled. In 1932, the National Research Council, in conjunction with the Empire Marketing Board, established the Institute of Parasitology for the study of parasitism in all its aspects. While maintaining the closest contact with the University, it is housed in a building of its own (provided by the Quebec Government), situated at Macdonald College. Parasitism is Empire-wide in its effects, and neither man nor any of his animals escape; so while the new Institute will investigate the subject particularly from a Canadian point of view it must, of necessity, form an important link in the new chain of science which binds the Empire together, and we may rest assured that the great spirit of Osler will watch carefully over its progress and destiny.

I wish to express my grateful thanks to Dr. Harvey Cushing, author of "The Life of Sir William Osler", for his permission to quote various passages from his book.

OSLER'S PUBLICATIONS, WITH ESPECIAL REFERENCE TO HIS CONTRIBUTIONS ON HEART DISEASE*

BY MAUDE E. ABBOTT, B.A., M.D.,

Curator of the Medical Museum,

McGill University, Montreal

I. *Statistical.*† Osler's literary output, as computed from the Classified Bibliography‡ of his publications, comprises some 1,420 items, of which 26 were in the field of Natural Science (published during his Canadian period), 429 in Comparative and Human Pathology, 555 in Clinical Medicine; 181 were Literary Papers,

* Abstract of a paper presented at the History Section of the College of Physicians, Philadelphia, on February 12, 1934.

† The figures in this paragraph are subject to final revision before publication of this Address, which will appear in the History Section of the *Johns Hopkins Hospital Bulletin.*

‡ Classified and Annotated Bibliography of Sir William Osler's Publications. Sir William Osler Memorial Volume and Bulletin No. IX of the International Association of Medical Museums, 1927, 2nd Edition, pp. 473-606.

162 on Medical Education, 70 on Public Welfare and 19 were Volumes Edited. For adequate evaluation of these it was necessary to differentiate between major and minor communications, *i.e.*, the form of publication. Analysis of the 1,420 items showed 461 major original articles (including 28 monographs and 13 books); 303 editorials, book-reviews, obituaries or published correspondence; 180 case-reports, notes and comments, etc.; and 279 specimens or autopsies reported. These figures, and others indicating his relative productivity in the four periods of his career, as also the details of his publications on cardio-vascular disease, were presented in tabular form as statistical charts and are very illuminating.

II. A short *Biographical Outline* followed, dealing chiefly with Osler's Canadian period and the formative influences of these earlier years (illustrated). In this connection the importance was stressed of his service as pathologist to the Montreal General Hospital (1876-1884), where he did over 750 autopsies and made the nucleus of a great pathological collection, the major portion of which, consisting of 150 specimens in perfect preservation, is still housed at the McGill Museum. Nearly all became the subject of articles published, and they are thus a bio-bibliographic asset of immense value.

III. *Osler's Contributions to Heart-Disease* constituted by actual count as well as in bulk of material nearly one-third of his publications on clinico-pathological subjects. Similarly, 80 of the above specimens, *i.e.*, over half of the 150 in the McGill collection, present lesions of the circulatory system and form a highly representative series, practically all of which formed the starting point for later investigations. As of special importance in this regard were cited his articles on "Aneurysm of the Hepatic Artery", "Overstrain of the Heart", etc. (1877); "Obliteration of the Portal Vein" (1879); "Of the Inferior Cava" (1879), and of the Superior Cava (1882: 1903); "Fibroid Degeneration of the Heart" (in angina pectoris) (1880); "Cases of Cardiac Abnormalities" (1880-1886); "Infections, so-called Ulcerative Endocarditis" (1881). Of prime importance were his Goulstonian Lectures on Malignant Endocarditis, based on 23 cases, 13 of which are seen preserved in this collection; and his great series of aneurysms of the aorta and its branches (28 specimens here). Again, "The Cardiac Relations of Chorea" (1887), a statistical study based on the records of the Philadelphia Infirmary for Nervous Diseases, traced its first impetus to at least two of these Montreal cases with autopsy, both of which are seen on the stand (slides).

So also his many articles and monographs on aneurysm, spontaneous, mycotic and dissecting, and his great Practice of Medicine itself are replete with references harking back to this early Montreal experience, the essentials of which are embodied for our inspection in the extraordinarily valuable Osler Pathological Collection of McGill University.

IV. *Personal Reminiscence.* This consisted in a short account of a visit of Dr. Osler to the McGill Museum in 1904 for the purpose of allocating references on certain specimens in his collection, and of an active correspondence that ensued on the literature on mycotic and dissecting aneurysm, on the progress of the Museum Catalogue, and on certain articles written by the author at his invitation on Museum Teaching* and Congenital Heart Disease.† Out of a total of some forty or fifty letters received by him on these subjects, five were selected for perusal here as illustrative of the great-heartedness of the man and of his whole-hearted encouragement of the junior worker.

Association Notes

The Sixty-fifth Annual Meeting of the Canadian Medical Association, Calgary, June 18th to 22nd, 1934

An event of interest will be the annual golf tournament in competition for the trophy cup donated by the Ontario Medical Association. This will take place on June 21st at the Calgary Country Club. Every registered member of the Canadian Medical Association and members of his family, will have the privileges of both the Country Club and of the Earl Grey Club golf courses. The Glencoe Club, the newest and best equipped for tennis and lawn bowling and indoor sports, will also open its doors to members of our Association.

G. E. LEARMONTH,
on behalf of the Local Publicity Committee, C. M. A.

The Dinner to Mr. Arthur Wood, of the Sun Life Assurance Company of Canada

We note with peculiar pleasure the occurrence recently of a function of more than ordinary interest. On Saturday, April 7th, the Executive, for itself, and on behalf of the Canadian Medi-

* The Museum in Medical Teaching. By Maude E. Abbott, *J. Am. M. Ass.*, 1905, **44**: 935.

† Congenital Cardiac Disease. *Osler & McCrae's Modern Medicine*, 1908, **4**: 323-425; *Ibid.*, 1915, **4**: 323-448; *Ibid.*, 1927, **4**: 612-812.

cal Association, entertained at dinner at the Montreal Hunt Club Mr. Arthur Wood, the newly-elected president of the Sun Life Assurance Company of Canada, and some of his colleagues. In the regretted absence from illness of Dr. A. T. Bazin, Chairman of Council, the dinner was presided over very ably by Dr. Alexander Primrose, of Toronto, who was in excellent vein. The guests of honour were Mr. Arthur Wood, Mr. E. A. Macnutt, Vice-president, Mr. George Bourke, Chief Actuary, and Drs. W. F. Hamilton and C. C. Birchard, Medical Referees, and some ten or more members of the Executive also sat down.

It is unnecessary to comment in detail on the great debt of gratitude which the Canadian Medical Association and, indeed, the whole medical profession of Canada, owes to the Sun Life Assurance Company. Through its active assistance post-graduate instruction has been brought to the doors of many who would otherwise have been deprived, at least to a great extent, of its benefits. This happy circumstance has been brought about by the institution of a system of travelling lectureships, a system which, we believe, has been in operation in no other part of the world. That the venture has proved an unmitigated success is attested by evidence from all over Canada. A pleasing feature of the banquet was the presentation to Mr. Wood, on behalf of the Canadian Medical Association, of a book, handsomely bound in gilt morocco leather, containing an Address and copies of letters and press comments laudatory of the Post-Graduate Tours and of the great Company that made them possible. These letters emanated from all the Provincial Medical Societies and from many local ones. The book will, we believe, be a pleasing and useful souvenir of a noteworthy undertaking. Doctor Primrose, in presenting the book, read the Address, and very gracefully voiced the appreciation of the Executive and Association of the work of the Sun Life Assurance Company. The reply of Mr. Wood was very happy, as he referred to the great altruism of the medical profession and their progressiveness and stated that his Company had been pleased to be of assistance in a particular way. He regretted that it had been impossible to keep on the good work, owing to circumstances of which we were all aware and from which we all had suffered. He was followed by Mr. MacNutt, who also spoke very happily. Other appropriate speeches were made by Dr. G. A. B. Addy, the President of the Canadian Medical Association, Dr. J. G. FitzGerald, Dr. F. N. G. Starr, and Dr. Gérin-Lajoie. The occasion proved to be a very delightful one and fittingly emphasized the cordial relations that exist between the Sun Life Company and our Association.

Hospital Service Department Notes

Medical Participation in Hospital Contracts

In most provinces in Canada there is legislation whereby municipalities pay specified *per diem* sums to public hospitals for the care of indigent or non-paying patients residing in such municipalities. Of recent years a tendency has been noticeable, particularly in some western provinces, for municipalities to contract with certain hospitals for the care of *all* non-paying patients from such municipalities. In making these arrangements a certain amount of "shopping" has been manifested. Inasmuch as emergency patients are frequently rushed to the nearest hospital, and many patients prefer to go, and do go, to other hospitals anyway, repeated difficulties have arisen between non-contract hospitals and municipalities, with the result that, in one western province at least, it was deemed necessary to pass legislation protecting the non-contract hospital required to accept such patients.

As a result of this contract arrangement and also that of certain cooperative hospital insurance plans, hospital staff members, who have been quite willing to give gratuitous medical care on the public wards to patients from their own districts, are finding that they are being asked to give such charity services to patients from other municipalities as well. As one prominent member of the profession, whose ceaseless and unpaid services to the poor over many years of practice will have earned him at least bushels of jewels for his heavenly crown, put it: "This is a bit thick!" Recently the Council of Physicians and Surgeons of Alberta brought this aspect of the contract arrangements to the attention of the Alberta Hospital Association and the Executive Committee of this latter body passed a resolution expressing its opposition to contracts providing hospitalization with medical service wherein the medical staff is not paid for the services rendered. The principle of the contract arrangement was not under consideration nor, apparently, was there any intention to prevent a hospital staff, for instance, that of a teaching hospital, from agreeing to undertake such free services of their own volition; but the president of the hospital association did seem to express the general opinion of his colleagues when he emphasized that "No hospital has the right to exploit the services of its medical staff".

This type of contract for indigent care should not be confused with the various forms of periodic payment or group hospitalization which

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

have been developed in so many centres in Canada and the United States, particularly during the last few years. These plans deal almost entirely with contributory groups of employed citizens, and in almost all instances the arrangement with the physician is a personal matter with the patient or is covered by a separate group arrangement.

Medical Societies

The Calgary Medical Society

At the annual meeting of the Calgary Medical Society, held on April 3, 1934, the following officers were elected for the ensuing year: *President,* Dr. A. H. Baker; *Vice-president,* Dr. F. T. Campbell; *Secretary,* Dr. A. J. Fisher; *Treasurer,* Dr. A. I. Danks; *Librarian and Historian,* Dr. G. E. Learmonth; *Executive Committee,* Drs. H. N. Jennings, J. W. Richardson, R. R. Hughes.

The Edmonton Academy of Medicine

A meeting of the Academy was held on February 7th in the Medical Building of the University of Alberta.

The scientific part of the program was introduced by Dr. J. A. McPherson who spoke on "The treatment of fractures and dislocations of the clavicle." After explaining the anatomical features involved in such injuries to the clavicle he proceeded to demonstrate on a subject the application of a posterior horizontal splint for fracture of the clavicle. This simple one-piece splint with a pad in the axilla, when affixed, fulfilled all the requirements of keeping the shoulder of the affected side, upwards, backwards and outwards, while it allowed the patient to go about comfortably dressed with the arm of the affected side free in its movements, a great advantage over the older and long used methods such as the Sayre plaster bandage.

Dr. I. R. Bell then gave a short talk on "Some recent advances in medicine". In his interesting report he referred to a new development in the production of smallpox vaccine, which is produced by growth on chick embryos, obtaining thus a pure sterile culture of vaccine, which promises to replace the calf vaccine for the prevention of smallpox. A new drug of considerable promise is "Dilaudid" which is a morphine derivative of equal value in the relief of pain, and with, apparently, no tendency to habit-formation. An old drug, *i.e.*, Ethyl Alcohol appears to be regaining somewhat its former prestige. Some recent work seems to indicate that this drug is of considerable value in increasing the circulation in the extremities and hence is valuable in the treatment of occlusive peripheral vascular diseases. This information, Dr. Bell remarked, would no doubt be received with considerable satisfaction and relief by a number of his confrères!

The final subject of the evening was an interesting talk, illustrated by lime-light views, by Dr. Jessie M. Allyn, K.I.H., who graduated from Toronto University Medical Faculty in 1904, and has spent 29 years in the service of Baptist Missions at Pithapuram, 280 miles north of Madras in India. Her subject was "An up-country doctor in India." In the Women's Hospital at Pithapuram, which is a training school for native nurses, she is carrying on a wonderful work in endeavouring to carry the gospel of modern medicine and surgery to the teeming millions of India, in the face of what appear to be the most discouraging and insurmountable obstacles, due to extreme poverty of the masses of the people, squalor and insanitary conditions, religious prejudices and fanaticism, difficulties due to caste, child-marriage of girls, and climatic conditions very trying to the white race. The tribulations and hardships borne by medical men in the remotest outlying districts of Canada pale into insignificance when contrasted with the lot of an up-country doctor in India. Cæsarean section is a very common operation, due to the extreme youth of many mothers. Her modest and unassuming presentation of the subject won the admiration of her medical confrères for the heroic courage, enthusiasm and happy acceptance of conditions which have enabled her to carry on so successfully and for so many years her chosen career in life. On furlough, Dr. Allyn is now visiting various centres in Canada and will return to her duties in India in the Fall. In her work in the hospital there she is assisted by her sister Laura, who is a graduate nurse.

At the meeting of the Academy held on March 7th the scientific part of the program was opened by a well-delivered paper on "The clinical significance of hæmaturia" by Dr. Emerson Smith, urologist. Two matters of great importance were emphasized by the speaker: (1) That the diagnosis of the cause of hæmaturia was very uncertain and liable to be mistaken unless to all the usual methods of examination a complete cystoscopic examination was added; and (2) that the less painful the symptoms associated with hæmaturia were, the more likely was the case to be very serious.

The followed a symposium on "Communicable disease," opened by Dr. R. B. Jenkins, M.O.H., who gave a scientific summary of the latest developments of preventive medicine. In referring to the recent almost complete abolition of diphtheria in Edmonton as a result of the campaign of preventive inoculations of school children, as well as many of earlier age,

for the last 10 years, he stated that, up to the present time, he had hesitated to advocate general inoculation as a preventive of scarlet fever, because of the danger of lessening the public confidence in the value of inoculation for diphtheria prevention.

He was followed by Dr. F. J. Folinsbee, specialist in children's diseases, who humorously related some of his own personal experiences with measles. In regard to measles, he stressed the importance of having the public realize how dangerous the disease was in the early ages from 1 to 5 years.

Dr. A. F. Anderson, Superintendent of the Royal Alexandra and Isolation Hospitals, completed the symposium by relating incidents connected with his experience in his earlier years of practice in the Province of Manitoba, stressing the mistakes in diagnosis so frequently made by physicians and the danger of cross infection in isolation and other hospitals noticed in his later years of experience as a superintendent. He also discussed methods of prevention of cross infection.

A most interesting discussion followed, in which a number of the members present participated.

T. H. WHITELAW

Montreal Physiological Society

At a meeting of this Society held on March 19th, the following papers were read, which are here given in abstract.

SOME ASPECTS OF LEAD EXCRETION, by R. U. Harwood, Ph.D.

Data obtained during studies in the Department of Neurology and Neurosurgery at the Royal Victoria Hospital were reported. Urine and stool specimens were analyzed and results were calculated on the basis of three-day specimens. The analytical methods developed by Aub, Fairhall, Minot and Reznikoff (Medicine Monographs, VII, 1926) were used.

The cases studied were, in general, patients with some neurological condition such as multiple sclerosis. It was found that urinary excretion on these hospital patients tended to be low. An average of 98 analyses on nine patients was 0.019 mg. per litre, with a range in these cases of 0.00 to 0.10 mg. per litre.

The effect of various therapeutic measures was also studied. In accordance with the results obtained in other laboratories, when an acidosis was induced by the administration of ammonium chloride a marked increase in lead output usually occurred, especially in the fæcal output. This was more marked if the acidosis was produced rapidly and the CO_2 of the blood was brought to above 40 vol. per cent, and if the patient was placed on a low calcium diet. Ammonium acid phosphate, potassium iodide and 1 unit per day of parathormone, used in certain cases, had little effect on the lead output. The excretion tended to be less on a high calcium, high phosphorus diet. Further studies are in progress.

SOME OBSERVATIONS CONCERNING THE EFFECT OF HISTAMINE ON THE SECRETORY FUNCTION OF THE STOMACH, by Armine Alley.

It was demonstrated on dogs with a Pavlov or an Armour pouch, and on dogs with œsophagotomy and gastric fistula, that the secretory effect of a standard meal or of sham-feeding was greatly diminished if these were given after the end of the gastric secretion on histamine (0.75 to 1.0 mg.). On the other hand, the peptic power of the gastric juice and the output of enzymes in these cases were greatly increased. Therefore it seems that histamine, being itself a stimulant of gastric secretion, inhibits the secretory effect, and increases the trophic effect of other stimuli which act chiefly through the parasympathetic nervous system.

The Sault Ste. Marie Medical Society

The Sault Ste. Marie Medical Society at its meeting on March 17th was addressed by Dr. John Mann, of Toronto. He demonstrated an improved type of obstetrical forceps which was made for him out of Algoma steel by local workmen. His address was entitled "The mechanism of labour in abnormal vertex presentation." He dealt with matters of diagnosis, of anæsthesia, and rotation, both manually and instrumentally. He gave a critical survey of the forceps of Smellie, Scanzoni, Kieland and others, finally demonstrating that designed by himself. The chief interest in his instrument lies in the fact that the handles move on a ball and socket joint independent of the blades, and yet the two parts may be locked at the will of the operator. This allows them to be applied to the child's head in posterior positions, so that the head may be rotated and then the handles are rotated and extraction takes place, as with the ordinary anterior position, without so much damage to the maternal soft parts. It was the opinion of the members present that this very ingenious instrument would find an important place in the armament of the future obstetrician.

The Western Ontario Academy of Medicine

A general meeting of the Academy was held at the Nurses' Residence of Victoria Hospital, London, on March 23rd. The speaker was Dr. W.J. Gardiner, of the Department of Physiotherapy of the General Hospital, Toronto. The attendance was over one hundred, of which some sixty were graduates and some forty undergraduates. The address was much appreciated

as the subject is one on which much attention is being focused at this time.

The speaker pointed out that there were cases which were made worse by manipulations, especially those of hysteria, tuberculosis, acute arthritis, and chronic osteophytic arthritis. The amount of force used need not be very great, the knack consisting in a knowledge of the exact amount required and also of the amplitude of motion required. Many cases do not require anæsthesia. When however the pain and spasm are considerable it is better to employ it. Nitrous oxide and oxygen, with just enough ether to give time for all necessary manipulations, was the best. The cases should be followed up and physiotherapy with heat and massage was advisable.

X-rays were shown of several conditions which were suitable for manipulation, and the appropriate manipulations were demonstrated on a normal subject; in the neck, the patient on his back, extension and rotation being applied; in the dorsal spine, the patient either sitting or lying down, manipulation following the examination in such a way that the patient is not aware of the operator's intention to apply force, and this can be done before the muscular resistance has had time to come into play. This manœuvre can rarely be repeated a second time.

Regarding sacro-iliac disease the methods of examination required to demonstrate pain in the sacro-iliac joint were described; by flexing the straight leg on the abdomen; by flexing both legs on the abdomen, with the leg either flexed or extended at the knee; with the patient lying on his face, the whole leg being dorsi-flexed on the back as far as possible; the patient on his side: with (a) the manipulator in front of him with the manipulator's elbow, which is closer to the patient's head, firmly fixed above the patient's axilla, so steadying the trunk, the manipulator gives a firm backward thrust to the pelvis; or (b) the manipulator at the back of the patient thrusts the shoulder forward, at the same time pulling the pelvis backward or passing an arm around the patient's flexed legs, and so rotates the pelvis upon the spine. As the force necessary in some of these cases is considerable, an anæsthetic may be required. This reduces muscular spasm and so the amount of force to be used.

Dr. F. J. H. Campbell moved a vote of thanks to Dr. Gardiner. This was seconded by Dr. G. Ramsay. The president, Dr. D. D. Ferguson, explained that it was not customary to propose a vote of thanks, but he allowed this to be done in this instance as the interest shown by the audience had been exceptionally great. On putting the motion to the meeting it was acclaimed with prolonged applause. E. SEABORN

University Notes

The University of Manitoba

THE JUBILEE CELEBRATION

In connection with the Jubilee Celebration of the University of Manitoba, a "Clinical Week" has been arranged, which promises to be most interesting and valuable. The program follows.

TENTATIVE CLINICAL WEEK PROGRAM

Monday, May 14th

9.00-12.00—Registration—Manitoba Medical College.
11.00-12.00—Moving picture — "Infections of the hand".
12.30- 2.00—Lunch—Clinical address.
2.30- 5.00—Fractures—Dr. H. P. H. Galloway, Chairman.
(1) Immediate care of fractures and transport of patient.
(2) Methods of applying traction.
(3) Fractures of the elbow in children.
(4) Fracture of the neck of the femur.
(5) The value of non-padded plaster casts.
(6) Reduction of fractures under local anæsthesia.
(7) Some end results of fractures—good and bad.
Evening—Ceremonial meeting and reception—Winnipeg Auditorium. Address: Progress of medicine in fifty years—D. A. Stewart.

Tuesday, May 15th

9.00-11.00—Clinical pathological conference—Prof. C. R. Gilmour and Prof. Wm. Boyd.
11.00-12.15—Small group clinical demonstrations and discussions.
12.30- 2.00—Lunch—Clinical address: Prof. R. L. McGibbon, Saskatoon: "Flights from medicine".
2.30- 5.00—Surgical emergencies—Prof. B. J. Brandson, Chairman.
(1) Treatment of head injuries.
(2) Diagnosis and treatment of abdominal injuries.
(3) Emergencies of upper abdomen.
(4) Late appendicitis.
8.30—Scientific meeting—guest speakers:
Dr. A. A. Fletcher, Toronto.
Dr. N. M. Keith, Rochester, Minn.: Management of ascites.
Dr. O. H. Wangensteen, Minneapolis.

Wednesday, May 16th

Morning—University of Manitoba Convocation—Winnipeg Auditorium.
Afternoon—Clinical lectures—medicine and surgery:
Dr. N. M. Keith, Rochester, Minn.: Essential hypertension.
Professor Wangensteen.
Evening—Alumni dinner and dance.

Thursday, May 17th

9.00-11.00—Tumour clinic—Prof. Wm. Boyd, Chairman.
(1) Grading of malignancy; its bearing on treatment.
(2) Lip and oral cancer.
(3) Cancer of breast.
(4) Enlarged lymph glands of the neck.
11.00-12.15—Small group clinical demonstrations and discussions.
12.30- 2.00—Lunch—clinical address.
2.30- 5.00—Functional disorders of the nervous system—Chas. Hunter, Chairman.

Friday, May 18th

9.00-11.00—Obstetrics and gynæcology—Prof. D. S. MacKay, Chairman.
(1) Obstructed Labour—O. Bjornson.
(2) Toxæmias of pregnancy—Ross B. Mitchell.
(3) Cancer of the cervix—J. D. McQueen.
11.00-12.15—Small group clinical demonstrations and discussions.
12.30- 2.00—Lunch—clinical address.
2.30- 5.00—Medical symposium:
(1) A short review of digitalis therapy and the use of modern diuretics—Prof. C. R. Gilmour.
(2) The modern treatment of anæmias—L. G. Bell.
(3) Essential hypertension—J. D. Adamson.
(4) Common types of diarrhœa in adults; their significance, diagnosis and treatment—Dr. H. D. Kitchen.
Evening—Gordon Bell Memorial Lecture—Prof. Wm. Boyd, under auspices of the Winnipeg Medical Society.

Saturday, May 19th

9.00-11.00—Diseases of children—Dr. Gordon Chown, and Dr. J. D. McEachern, Chairmen.
(1) The acute abdomen in children.
(2) Pyuria in childhood.
(3) Some aspects of tuberculosis in childhood.
(4) The acute ear in childhood.

Small Group Clinics and Demonstrations

Heart—John M. McEachern.
Varicose veins and ulcers—C. E. Corrigan, and Dr. Ross Cooper.
Clinical laboratory methods—Daniel Nicholson.
Diabetes—A. Hollenberg.
Infant feeding—Gordon Chown.
Nephritis—Prof. Wm. Boyd; L. G. Bell.
Rectal surgery—P. H. T. Thorlakson.
Dermatology—A. M. Davidson.
Goitre—Gordon Fahrni.
Obstetrics: Pre- and post-natal care—Blake Watson.
Mechanism of labour—A. Blondal.
Face and brow presentations—W. G. Campbell.
Use and abuse of forceps—F. G. McGuinness.
Hæmorrhages of pregnancy—C. L. Arthur.
Methods of induction—A. S. Kobrinsky.
Gynæcology: Radium and the cautery in cancer of the cervix—J. D. McQueen.
Irregular bleeding at the menopause—Prof. D. S. MacKay.
The Friedman pregnancy test—Blake Watson.
Diagnosis and treatment of common cervical conditions—C. R. Rice.
Trichomonas vaginalis—C. W. MacCharles.
Chest—D. L. Scott; M. B. Perrin.
Eye—Prof. T. Herbert Bell.

Dr. A. MacLean (Man., 1934) and Dr. C. F. Code (Man., 1934) have been awarded three-year fellowships under the Mayo Foundation at Rochester, Minn., on account of general proficiency. Both are now completing their intern year at the Winnipeg General Hospital and will begin their fellowships during the summer. Dr. Code will study in the Department of Experimental Medicine, while Dr. MacLean, a son of the President of the University of Manitoba, will study in the Department of Clinical Medicine.

Special Correspondence

The Edinburgh Letter

(From our own Correspondent)

In view of the widely prevalent view that an abnormally heavy rainfall is a constant feature of the Scottish climate, it is interesting to note that a considerable number of districts in Scotland are threatened with a shortage of water. In view of the importance of an adequate supply of pure water from the public health point of view the Departmental Committee on Health Services, which is at present sitting, has issued an interim report on the subject. The large centres such as Edinburgh, Glasgow, Aberdeen, and Dundee have sufficient reserves to meet the situation, but the position of many of the smaller towns and rural districts is causing some anxiety. The report recommends that a survey of the whole water supply of Scotland should be instituted at once. There is no doubt that, given proper organization and coordination, the water resources of the country are adequate to meet all demands. There has been a marked increase in the consumption of water of recent years. This is due in part to the development of housing schemes and to a greater appreciation by certain sections of the population of the value of personal cleanliness from the health point of view. It appears that the dry conditions experienced during the past winter have been caused by the same persistent high-pressure area on the Atlantic as maintained the dry, hot weather during the summer.

Since October 1, 1931, the capitation fee under the National Health Insurance Acts has been subject to a deduction of 10 per cent. This deduction was voluntarily accepted by the profession at that time as part of their contribution to meet the national economic situation. Now that the financial condition of the country is showing signs of improvement there has been a movement by various other bodies who also suffered temporary deductions from their remuneration, to take steps to have these deductions restored. A deputation from the Insurance Acts Committee of the British Medical Association recently met the Minister of Health and pointed out that the matter was one which should be given urgent consideration by the Government. The Minister of Health in his reply stated that the question as to whether or not the time had come when the economy cuts could be restored was one on which only the Chancellor of the Exchequer could pronounce. He assured the deputation, however, that as soon as the appropriate time arrived, there was no danger of the interests of the insurance practitioner being in any way postponed or overlooked.

The organization of schemes to assist in the early diagnosis and treatment of cancer is re-

ceiving a large amount of attention at the present time. At a public meeting, held recently in Edinburgh under the chairmanship of the Lord Provost, it was resolved to form a Cancer Control Organization for Edinburgh and the south-eastern region of Scotland. The increase in the incidence of the disease is apparent from the fact that the deaths from cancer in Edinburgh in 1898 were 265, and in 1933 the number was 785. Mr. J. J. M. Shaw, F.R.C.S., who outlined the scheme, said the practical issue was the elimination of delay. Valuable time might be lost from the time the patient first noticed something wrong with himself to the time when his first visit was paid to the doctor. It was proposed that there should be judicious dissemination of knowledge as to when the doctor's advice should be sought, and that through the medium of nurses, welfare workers, health visitors, and meetings of those who desired information, some indication should be given of changes which might suggest the development of malignant disease. He emphasized that it was not necessary that the lay public should be instructed as to what were the symptoms of cancer. All that was asked was that they should take warning of any change of habit or form of the body. The public should also be told that, contrary to a large amount of popular opinion, there was no stigma attached to cancer and no suggestion of any family inferiority—a thing which kept many people from seeking advice. Mr. Shaw referred to the argument that education of the public in the matter might produce undue fear by saying that cancerophobia was already present, and arose much more from ignorance than from knowledge. What they were asking was that people should read carefully the traffic signals on their road of life. An executive committee was formed to take the necessary steps to secure team work in the attack upon the disease, including affiliation with Imperial and International organizations.

By the death of Dr. David Lees the medical profession in Scotland has lost an outstanding personality. He was a well-known authority on the subject of venereal diseases and rendered valuable services as the surgeon in charge of the venereal disease department of the Royal Infirmary, Edinburgh. He was also the Lecturer on this subject in the University. A few years ago he was invited to visit India to advise the Government with regard to the treatment of venereal disease. He was a generous, big-hearted man who dealt with the special difficulties which constantly arose in the course of his work in a most helpful way. Many a wanderer from the paths of rectitude has been put on the straight road by his quiet talks. He used to say "my job is to heal the sick, not to condemn the sinner", and he invariably observed this principle. He took a keen interest in many varied aspects of life and his passing leaves a blank which it will be impossible to fill.

R. W. CRAIG.

7 Drumsheugh Gardens,
Edinburgh.

The London Letter

(From our own Correspondent)

The most important event of the past few weeks has been an official statement on the present position and future policy of the British Post-Graduate Medical School. From time to time mention has been made in these notes of the progress at Hammersmith, on the western outskirts of London, where the foundation stone of the medical school buildings was laid last July. The Dean of this very important new institution, Dr. M. H. Mackeith, came from Oxford at the beginning of this year to take up his duties and following the recognition by the University of London of the new school the four main "chairs" have been advertised. These are for professors of medicine, surgery, of midwifery and gynæcology, and of pathology. By arrangement with the London County Council, who control the Hospital with which the new school is associated, the holders of the chairs of the three main clinical subjects will have general charge of the beds and will also be provided with facilities for original investigations. Research laboratories will also be available, while for the pathological department there is planned more generous laboratory accommodation for the three main divisions, morbid anatomy, biochemistry and bacteriology. As soon as the holders of the main chairs have been appointed more detailed organizations can be proceeded with, and in the Dean's statement it is notable that great stress is laid upon the importance of a really high level for the teaching. It is proposed that eminent physicians and surgeons not permanently attached to the school will deliver courses of lectures from time to time and all the existing facilities for post-graduate medical teaching in other centres throughout London will continue to be made use of. The governing body can now proceed rapidly towards the provision of the early stages of the work at Hammersmith and the future development should be rapid.

Great interest has been attached by certain organs of the lay-press to an out-spoken article in a medical journal by one of London's surgeons on the question of certain hospital customs which he characterizes as "anachronisms embodying some of the most barbaric features of the Middle Ages". The matter might be thought to have merely a domestic interest were it not for the very large number of letters printed day after day in the press from lay-sources agreeing with the criticisms and voicing others, indicating that

from the point of view of the public our hospitals are in need of radical reform in many respects. The main "anachronisms" quoted in the original article were the customs of allowing patients to die in a public ward and of allowing operation cases to recover from anæsthesia also in a public ward. The suggested remedies for these two evils were the provision of a small ward for the dying and of a special recovery room. Economic considerations apart, the case for the latter is unanswerable but the former carries certain disadvantages from the psychological aspect. Other suggested reforms include the provision of better accommodation for patients who are up for a portion of the day, such as dining rooms and sitting rooms, adequate convalescent home treatment for patients at a much earlier stage than at present and also an efficient follow-up system. Perhaps to readers in Canada these suggestions for the hospitals of the future will suggest that in London institutions are hopelessly out-of-date. This is not altogether true, but the question is a complex one, especially in view of the possible and indeed probable development of the municipal hospital in the coming years.

This possibility has an added interest after the results of the recent London County Council elections in which the Labour Party secured a majority for the first time. In the program issued by this Party before the election reform of the hospital and public health services was stressed as one of the urgent tasks to be undertaken. Medicine is well represented in the new Council, for all ten of the medical men and women who stood as candidates were elected, and one of them, Mr. Somerville Hastings, an ear, nose and throat surgeon, has been appointed chairman of the newly constituted hospitals and medical services committee. The extent of the health services provided by the Council can be realized from a consideration of the following figures based upon the most recent annual report. During the year 260,000 patients were admitted to the Council's hospitals, and at the end of the year 35,000 patients were actually occupying beds in its general and special hospitals, including sick-beds in the public health and public assistance institutions. The "district medical services", comprising domiciliary medical care previously provided under the old "poor law", meant during the year a total of over 70,000 visits. Another aspect of the work was represented by the infectious fevers hospitals in connection with which over 100,000 examinations for diphtheria bacillus by serum cultures were made during the year. There is also the school medical service, the London Ambulance Service, etc., and the total staff, including part-time and whole-time officers engaged in the health services of the Council, is over 18,000. Already the envy of many other cities, here and abroad, this is the organization which is to be improved by the new Council!

ALAN MONCRIEFF.

121 Harley St.,
London.

Letters, Notes and Queries

The Danger from Dinitrophenol

To the Editor:

In a recent communication to this *Journal* (1934, **30**: 128) attention was drawn to experiences with dinitrophenol and its allied compounds. Some of these compounds are remarkable metabolic stimulants; they may raise the metabolic rate to a very high level within an hour, and, for this reason, have been recommended by some for the treatment of obesity. In the above communication, particular attention was drawn to the difficulty of predicting the toxicity of this drug. The same amount may not only affect people of the same body weight differently, but it may act differently in the same person on different days. Because of their irregular action it was suggested that the use of such drugs should as yet be confined to hospital practice, where, with proper laboratory facilities, they can be carefully controlled. This was not the first warning. Attention has been drawn repeatedly to the possible harmful effects of these compounds by those who have had experiences with them, and also in editorial comment in a number of journals.

Since the publication of the above-mentioned paper, I have received twenty-two letters from physicians in practice requesting information about the purchase of dinitrophenol, and it is of interest to note that, of these requests, 16 were received from physicians who have little or no access to basal metabolism tests, without which the action of this drug cannot be properly controlled. The importance of these tests is emphasized by the fact that one of the characteristics of this drug is that its action is not reflected in the pulse rate, unlike in thyroid medication; the pulse rate may remain normal in spite of a marked increase of metabolism.

A number of deaths from dinitrophenol have already been reported. During the last few weeks alone three were recorded—two in the *Journal of the American Medical Association* of April 7th, and another in the *British Medical Journal* of March 24th, p. 539. Deafness was reported in another case (*J. Am. M. Ass.*, 1934, **102**: 838); seven months after the drug was discontinued there was still considerable impairment of hearing. In a recent editorial in the

Answers to questions appearing in this column should be sent to the Editor, 3640 University Street, Montreal.

Journal of the American Medical Association (1934, **102**: 1156) attention was drawn to the fact that, as is usual with drugs for cosmetic purposes, commercial interests have entered the field and vast numbers of people are taking these nitro compounds without advice from physicians.

Apart from the necessity for effective legislation to control the sale of these drugs, there is a medico-legal aspect which concerns physicians. Law courts do not demand infallibility on the part of physicians, but they do demand exercise of reasonable care and judgment. As the importance of basal metabolism tests has been emphasized repeatedly, the physician who uses these nitro compounds without such tests is exposed to the charge of negligence. Even with access to these tests, it is important to warn patients of the possible harmful effects of the drugs and, in doing so, to point out the different manifestations of toxicity, particularly skin rashes, pruritus and fever. Finally, in the opinion of the writer, this drug should be used only when all other and more safe methods of treatment of obesity have been given a reasonable trial and have failed.

I. M. RABINOWITCH.

Montreal General Hospital,
April 11, 1934.

Topics of Current Interest

Aspirin Poisoning

Aspirin is an organic compound, synthesized from salicylic acid, itself a synthetic drug. The physiological action of aspirin resembles that of salicylic acid, except that its untoward effects on the stomach are relatively slight, the salicylic radical not being split off until it reaches the alkaline medium of the intestine. For this reason it is better to administer it in a neutral medium; *e.g.*, in a tumblerful of water, whereas we usually combine the pure salicylate with an alkali, such as potassium bicarbonate.

The depressing effect upon the heart of acetyl-salicylic acid (aspirin) is not nearly so marked as that of the ordinary salicylate. Its action on unstriped muscle, however, is decidedly excitant, as shown by its toxic manifestations, such as, angio-neurotic œdema, urticaria, vaso-motor spasm, spasm of the glottis, etc.

The toxic dose of acetyl-salicylic acid varies greatly with the individual. In some, very rarely, fortunately, there is what amounts to an idiosyncrasy. And it is with this, primarily, I am concerned in this article, as three such cases were treated by me during the past two or three months.

CASE 1. NOVEMBER, 1933

A male, aged 30, well nourished; no medical history of any kind. He purchased a couple of capsules at the drug store for a "cold". These were stock capsules put up by a reliable house and contained 3¼ gr. aspirin, with a small quantity of phenacetin and caffeine. He took these at night along with the conventional hot lemonade. I saw him on the following early morning. His temperature was sub-normal; pulse 70, of good volume. His face and eyelids were markedly œdematous, large urticarial wheals extended over neck and chest. Œdema extended to the hands and fingers. He complained only of the itching. The urticaria cleared up in less than twelve hours, but his face and hands remained œdematous for three or four days. He claimed that the capsules had poisoned him, as he began to feel "queer" fifteen or twenty minutes after swallowing them. I concurred in his diagnosis.

CASE 2. NOVEMBER, 1933

A male, aged 27; no medical history of any kind. He was seen by me about 8 p.m. He reported having taken two 5 gr. tablets of ordinary aspirin, some hours previously. He had practically the same symptoms as Case 1, and cleared up rapidly under eliminative treatment.

CASE 3. JANUARY, 1934

A housemaid, aged 24; medical history irrelevant; well nourished; intelligent. Her mistress had given her one of the same sort of capsules mentioned under Case 1. When I saw her about three or four hours after, her temperature was subnormal; pulse 120. Her face and eyelids were enormously swollen, urticarial wheals over neck and limbs. Her breathing was stridulous. She claimed that the capsule had poisoned her, as her face and neck began to feel "queer" a few minutes after taking it. She reported a previous attack, following ingestion of one "compound" tablet. At that time only her eyes were affected and this had cleared up by the next day. She was put to bed with hot water bottles and given a teaspoonful of spiritus ætheris nitrosi, repeated in four hours. In the following morning her temperature was 98 degrees; pulse 52; the urticaria and laryngeal stridor had cleared. The œdema persisted for two or three days, and gradually disappeared.

The toxicology of aspirin is rather obscure, so that no specific has been evolved for the treatment of these cases. Symptomatic treatment—vaso-dilators, amyl nitrite, nitroglycerin, strychnine, etc., would seem to be indicated.

Death has been reported from overdose of the drug. Authorities claim that its combination with quinine is dangerous, others that the combination with any of the coal tar derivatives is more toxic and depressing than when the drug is taken singly.—A. K. Roy, North Sydney, in the *Nova Scotia Medical Bulletin*, 1934, **13**: 76.

Report of the Committee on Educational Policies of the Association of American Medical Colleges*

The Committee on Educational Policies, after consideration of a provisional report on Medical Education and the Reform of Medical Studies, which was submitted to the Health Committee

* Presented at the executive session of the forty-fourth annual meeting of the Association of American Medical Colleges held in Minneapolis, October 31, 1933.

of the Health Organization of the League of Nations in Geneva last October, approved and recommended the following principles regarding medical education.

1. That medical education should train the student in the cultivation of health, in the prevention of disease, and in the practice of medicine, both individualistic and organized.

2. That the main purpose of undergraduate medical courses is to train "the basic doctor" by a basic medical curriculum; that is to say, the practitioner, capable of thinking for himself, endowed with initiative and resourcefulness, suited to the needs of modern society and the new forms of medical practice, and ready to be ripened by experience and life after he graduates.

3. That in the basic curriculum consideration should be given to replacing the quantity of the subjects taught by the quality of the knowledge to be acquired, the overextensiveness by thoroughness. The tendency to turn out the doctor who is a walking encyclopædia of medical science should be avoided.

4. That scientific instruction and clinical experience, theoretical teaching and practical application, university laboratories and hospital services, academic freedom and apprenticeship under guidance, should be made complementary to one another in the institution, the curriculum, and the methods of instruction.

5. That it is essential that there should be a liaison and exchange between the pre-clinical scientific period and the clinical period of the course, the teaching of the fundamental sciences being continued into the clinical part of the course, and the broad clinical principles being introduced in the pre-clinical period.

6. That the instruction in the pre-clinical sciences should be governed by the following principles:

(a) That, as the purpose of medicine is the promotion and cultivation of the health of people in addition to the treatment of sick patients, a thorough knowledge of the normal living, growing, and functioning being is essential.

(b) The basic course in anatomy should provide the student with a sound general knowledge of the structure of the normal human being in a state of health. Much of the detailed knowledge which is essential for special fields of practice, but not for a basic course, should be omitted. A greater coördination with physiology and the functional activity of structures as well as with the clinical subjects should be introduced.

(c) The increasing importance of physiology as a fundamental subject of medical education, as an experimental science, as a key to clinical training, as a means towards improving early diagnosis and treatment, and as a knowledge of the body functions in the normal healthy man, should be realized.

7. That clinical instruction should remain as the centre of gravity of the whole medical course, where a synthesis of all theoretical, scientific, and clinical principles should be effectively carried out.

8. That clinical instruction in each year should include the presentation of the subject where applicable from the standpoint of its relation to hygiene, to social service, to public health (including the care of indigents), to insurance (accident and life), and to industrial and community practice.

9. Specialization:

(a) That the training of the "basic doctor" should include only the main fundamental principles of the specialties needed by the general practitioner.

(b) That the training for the specialties should be provided for by the organization of graduate courses of instruction.

(c) That the determination of the qualifications of specialists to practise in a special field should be based on the fulfilments of certain minimum educational requirements and the passing of a specialist examination.

(d) That the possession of the necessary qualifications be recognized by a non-compulsory certificate or diploma and by the publication of a register or list of those holding such specialist certificate.

(e) That the supervision of the qualification and certification of specialists be placed under a board or council, consisting of representatives of the medical practitioners, the medical associations, the medical licensing bodies, and the universities.

Standardized Education

"Progress," said Sir Arthur Eddington, at the end of his Godlee lecture recently, "should be measured not by the questions we answer but by the questions we ask." By this criterion medical education must have made a great deal of progress in recent years, and by any other test we have every reason to believe that it has. The men and women who now leave our training schools are probably better equipped for their professional lives than they have ever been before, and this advancement gives fresh questions room to come to the front. One of the most interesting was asked by Sir Cuthbert Wallace, when recently he gave the Hunterian oration at the Royal College of Surgeons of England. Is it possible, he says, that we have gone too far in standardizing medical education? Might it not be better to allow individual schools sufficient freedom to develop their own characteristics? And he points out that under the existing uniformity no one education authority is doing what it really believes to be best. The position seems to be much the same as with the language in which we speak and write. To allow a British child to grow up in ignorance of any tongue but Welsh or Gælic is as criminal in our

modern world as to start it off without the multiplication table and a knowledge of reading and writing. But the standard English which has permeated the country through elementary education and the newspapers has its losses as well as its gains. That it facilitates intercourse is obvious, and in a practical world it may seem wholly to the good that Herefordshire and Yorkshire and even the Lowlands should be able to understand one another without enough trouble to make conversation something of an adventure. But the gain is made by a deplorable impoverishment of our vocabulary, and our centralized language has thrown overboard and is rapidly forgetting all about those vividly expressive words which enrich every brand of homely dialect. It may be convenient that a foreigner who has learned to read the *Manchester Guardian* will have no further difficulty with the *Yorkshire Post* or the *Glasgow Herald*, but it is sad to hear from an authority that much of Burns will soon be unintelligible to all but a few scholars. The individual language of the Bible and the Prayer Book still survives but it seems to be losing ground.

Everyone will agree that there is a certain common minimum of knowledge which must be made compulsory for all who aspire to practise medicine, and that this must reach beyond the analogues of reading, writing, and arithmetic. But it is surely unnecessary that it should extend to what may be called the sixth form work as well. At present no student is free till his name is on the Medical Register, and the possibility of self-determination is one of the most pleasant experiences of those who qualify. Up to this consummation any degree of personal freedom within a medical school is hardly feasible except for those of exceptional intellectual capacity. But there is no necessity that the ideals of the schools should be restricted to the same extent. In fact the London schools give an exaggerated impression of uniformity; in the provinces, where each university conducts its own examinations, there is more individuality which cannot develop in London, where not even the largest schools are allowed to escape the drab conformity of examinations over which they have no control. Elsewhere the courses of teaching and learning are not all the same, nor is the general colour of the schools altogether monotonous. The predominance of physiology at Oxford is almost an extravagant example; nearly all Oxford graduates may be expected to carry with them at least traces of the unequalled course directed by Burdon-Sanderson, Gotch, and Sherrington. But a similar if less conspicuous difference will be found between the men from Liverpool, Leeds, and Glasgow; they have been brought up in schools where values are not exactly the same and the product has a perceptible variety.

That there should be this variety we believe, with Sir Cuthbert Wallace, to be wholly to the good. Sincere people doing their best to devise the perfect curriculum will agree in all details only at the cost of unworthy compromise. Sincere teachers can standardize their teaching only by the sacrifice of those personal ideals and characteristics by which alone teaching can inspire. Within reasonable limits, let each go his own way. Most medical students come away from their schools with the impress of some particular teacher who happened to attract them and to whose teaching they attach exceptional importance. This fortunately is beyond the control of any central body. The same liberty can surely be allowed to the schools.—Leading article in *The Lancet*, 1934, **1**: 406.

Abstracts from Current Literature

Medicine

The Treatment of Allergic Diseases in General Practice. Bray, G. W., *Brit. M. J.*, 1933, **2**: 43.

An allergic individual is defined as one who shows exaggerated susceptibility to substances—chiefly proteins, but also to certain carbohydrates, drugs and physical agents—which are innocuous to normal persons in the amounts normally encountered. The hypersensitiveness may manifest itself as asthma, hay fever, eczema, urticaria, migraine, etc. "Allergy" is usually inherited, but may also be acquired, as the result of tissue damage or excessive irritation. If it arises in childhood, the hereditary factor is usually strong; when the manifestations first appear in adult life the post-natal factors have been severe. In nearly all secondary, acquired, cases, the allergic factor is either inhalant or occupational in nature. Hence the importance of a careful history in determining the etiology. Practically all allergic diseases are periodic, with intervals of complete freedom. Treatment resolves itself into emergent, during the attacks, and prophylactic, during the free intervals.

In the treatment of asthma, the first requisite is to determine the cause. A careful history may accomplish this. Skin tests, best carried out by an expert, may be necessary. A basic diet, free of all possible irritants should first be given, and then the possible offending foods added one by one, watching for reactions. Foci of infection should be removed, as reflex irritation will provoke attacks. It should be remembered however that nasal abnormalities are frequently the result of asthmatic attacks and not the cause. Desensitization may be attempted,

using either a mixture of inhalant allergens or a non-specific, as Witte's No. 30 peptone. Ephedrine is often useful in warding off attacks. Glucose helps some cases. Calcium is of no value.

Seasonal hay fever is only successfully treated if all possible allergic causes are recognized. These include not only the pollens of the locality, but also feathers, house dust, animal hairs and orris-root preparations. The pre-season method is best, starting three months before the season, with weekly injections; when the maximum dose is reached, it is advised that treatment be continued perennially (one injection each month for about three years) when all sensitivity will frequently be found to be lost. Co-seasonal treatment may be carried out, if necessary, by giving increasing pollen injections every two hours during the day. Two-thirds of cases are benefited. Vaccines and non-specific injection therapy are a waste of money.

Infantile eczema is a very common allergic manifestation. Most of these infants are sensitive to egg and often to other foods they may be getting through the mother's milk. The papular urticaria of childhood is extremely common in England. It has been stated to be due to dentition, constipation, improper feeding, uncleanliness, or to be an allergic reaction to environment. It disappears if proper care is taken with the dietary. Some cases of enuresis have been found by the author to be closely associated with allergic phenomena and to cease when these phenomena are treated. Ephedrine, gr. ½, early and again late in the evening, has been effective in many cases. W. FORD CONNELL

Aspirin Allergy. Duke, W. W., *J. of Allergy*, 1933, **4**: 42.

The effect of aspirin in an aspirin-sensitive person can be a catastrophe in every sense of the word. In one case, death followed the taking of an aspirin tablet. It has been stated that 10 per cent of asthmatic persons are sensitive to aspirin. Very few aspirin-sensitive persons give positive skin-tests to aspirin. Before giving aspirin to an allergic person one should know from the previous experience of that patient that aspirin is well tolerated, or one should test for sensitivity. The test is made by the breaking of several fragments from an aspirin tablet and placing one on the patient's tongue and having him move it around his mouth. A violent attack of cough, asthma, and itching may be precipitated within one minute. The attack can be stopped within a minute or two by having the patient rinse his mouth repeatedly with a solution containing four cubic centimetres of dilute acetic acid or vinegar to a glass of water. This removes the aspirin mechanically and stops its absorption. (Aspirin is insoluble in water and in dilute acid and is soluble in alkaline media such as the saliva). The symptoms produced can be further controlled by adrenalin if necessary. T. G. HEATON

Massive Anaphylactic Gangrene. Irish, H. E. and Reynolds, E. C., *J. Am. M. Ass.*, 1933, **100**: 491.

The occurrence of gangrene in sensitized subjects has been known since Arthus in 1903 reported his experiments. The author reports a case of gangrene of the buttocks following the therapeutic intramuscular injection of anti-meningococcus serum into the buttocks. He notes the occurrence of 2 previously reported cases, both of which followed the use of diphtheria antitoxin in persons sensitized by toxin-antitoxin, eight and four months previously (respectively). The author's case was a boy of 28 months who had received toxin-antitoxin nineteen months previously. Six injections of anti-meningococcic serum were given intramuscularly over a period of 13 days. The fourth injection was followed by blanching of the skin at the site of injection, and by generalized urticaria and fever. The sites of the fifth and sixth injections became purple. These lesions developed within 5 days into areas of gangrene, with discharge and sloughing in both buttocks and the sides of the abdomen and thighs. Death followed 3 weeks later. T. G. HEATON

Surgery

Post-operative Nutritional Œdema. Jones, C. M. and Eaton, F. B., *Arch. Surg.*, 1933, **27**: 159.

The purpose of this paper is to present evidence that nutritional œdema is not uncommonly associated with surgical procedures, particularly of the gastrointestinal tract.

The results of the authors' investigations were based upon the study of the case records at the Massachusetts General Hospital of 34 patients, 26 of whom showed œdema of greater or less extent. Of the 26 with œdema 21 showed disease of the digestive tract; 2 had carcinoma of the pancreas; and 3 required surgical intervention because of abscess of the lung, cancer of the ovary, and sepsis of a joint, respectively. Œdema of the nutritional type is considered to be associated with under-feeding and frequently with starvation; protein intake is ascribed as a cause, and the comparison between such œdema and that seen in the so-called "nephrosis" has been commented on. Experimentally, a relationship has been shown to exist between the production of œdema and a lowering of the serum protein, in association with excessive amounts of water and sodium chloride.

The authors divide their cases into two classes: (1) those with obvious œdema, and (2) those with potential œdema. In 17 of the 26 patients with obvious œdema there was a preceding history of anorexia, undernutrition, or vomiting, of

several weeks' duration. The post-operative œdema began as a rule about seven days following the operation, but as early as two days and as late as fifteen days after. Where there was moderate œdema it was in the legs, ankles or genitalia; where there was marked œdema it occurred in the peritoneal cavity, the walls of the digestive tract, and the mesentery and lungs. In the 8 cases of potential œdema there was marked undernutrition. The observation is made that, in spite of an apparently normal level of serum-protein, œdema may be produced rapidly by the administration of amounts of salt-containing fluid that would ordinarily cause no trouble. Extreme malnutrition and dehydration must be factors for such an occurrence.

As to prevention and treatment, there should be a limitation of the quantity of fluids and salt administered in cases showing definite malnutrition before operation. Preliminary determinations of serum-protein and chlorides should be made. Where undernourishment is marked, a preliminary gastro-enterostomy is advised, to permit a satisfactory protein intake for some days, until the serum protein has been raised above the critical level. Milk, egg-albumin and gelatin are of value. With post-operative intestinal œdema an attempt should be made to raise the serum-protein by limiting the intake of water and salt or alkali, or by producing diuresis. Repeated blood transfusions are of some immediate value where it is not possible to feed large amounts of protein, and should be used even in the absence of anæmia. Intravenous injections of concentrated solutions of dextrose are of value in producing diuresis.

G. E. LEARMONTH

Electric Shock. Pearl, F. L., *Arch. Surg.*, 1933, **27**: 227.

In electric shock, the chief issue is the unconscious victim, whose life on the instant is seriously threatened or already spent. The factors involved in the effect which a certain current will have on an organism are (1) tension or voltage; (2) intensity or amperage; (3) the type of current; (4) the resistance at the point of contact; (5) the path of the current, and (6) the individual susceptibility of the organism.

Currents of as low as 40 and 60 volts have caused death. It is now conceded, on the basis of experimental work, that, with currents alternating at ordinary rates (from 25 to 300 per minute), voltages under 220 tend to produce ventricular fibrillation, without affecting the respiratory centre; those over 1,000 tend to produce paralysis of the respiratory centre, without affecting the heart; and those between 220 and 1,000 tend to involve both the heart and the respiratory centres.

High tension currents are less dangerous than low tension ones. Alternating currents are said to be from three to four times more dangerous than direct currents. On the resistance of the skin is dependent the effect of the current on the body, and this resistance, in turn, depends on the dryness, cleanliness and thickness of the skin, there being more resistance where the hand is dry and much greater if calloused. The resistance is reduced when there is perspiration. The skin is the most resistant tissue of the body. In fatal injuries nearly all currents which traverse the head also pass through the chest. Currents from foot to foot are never fatal *per se*, no matter how great the current; but even a small current passed through the chest may cause death. Death has been shown experimentally to occur, (1) from primary fibrillation of the ventricles; (2) from failure of the respiratory centre; (3) from ventricular fibrillation combined with paralysis of the respiratory centre; (4) from prolonged tetanus of the respiratory musculature, or (5) suddenly, some time later—"delayed death".

Post-mortem findings fail to elicit the cause of the death changes due to electricity; vascular changes are noteworthy. Heat rather than electrolysis is probably responsible for most pathological changes. The treatment of failure of the respiratory centre is artificial respiration by the prone pressure method, until the victim breathes or until death is certain. Early resort to cardiac massage is advised when ventricular fibrillation is present. Proceed by the intraventricular injection of potassium salts followed by calcium salts. Inhalation of carbogen is a valuable adjuvant to artificial respiration. In some instances lumbar puncture is of value.

G. E. LEARMONTH

Obstetrics and Gynæcology

The Incidence, Treatment and Mortality of Eclampsia. Bender, J., *Am. J. Obst. & Gyn.*, 1934, **27**: 59.

The study was based on 13,354 patients in the obstetric department of the Jersey City Medical Centre and the Margaret Hague Maternity Hospital from July 1, 1926, to October 19, 1932, in which there were 123 cases of eclampsia. The conclusions reached are that pre-natal care, early recognition of toxæmia, and early hospitalization had decreased the incidence of eclampsia from 1 in 74 to 1 in 154. The mortality among clinic patients was 5.8 per cent, as compared with 15.3 per cent among patients who had not attended the clinic. Analysis of the radical and conservative phases of treatment was in favour of the conservative treatment, in that there was a marked decrease in maternal mortality from 17.7 to 7.7 per cent, and in gross fetal mortality from 44.3 to 27.1 per cent. Cæsarean section in the eclamptic should be reserved for pelvic indications. Low forceps and

episiotomy to expedite the second stage of labour did not increase the mortality. Spinal anæsthesia was considered to be the anæsthesia of choice. ROSS MITCHELL

Evaluation of Radiation Therapy in Malignant Disease of the Female Generative Tract. Healy, W. P., *Am. J. of Obs. & Gyn.*, 1933, **26**: 789.

In the treatment of malignant tumours of the female pelvis, radium and x-ray play a very important part. Although variations in radiation technique are great, and the response of different tumours to similar treatment is not always what we expect, yet certain methods of treatment, may be adhered to. The end-results are influenced by the patient's age and general condition, the extent of the disease, and also by the histological structure of the growth. From the standpoint of cure, the crux of the problem depends chiefly on the clinical stage of the disease.

Carcinoma of the vulva.—This is usually a fully developed epidermoid growth which occurs in women beyond the menopause and is radium-resistant. For this reason vulvectomy with dissection of the inguinal glands or more recently vulvectomy with heavy x-ray dosage of the groins is recommended and the results seem encouraging. *Vagina.*—This, too, is an epidermoid growth, and one in which surgery had proved very disappointing. Radiation with both radium and deep x-ray is advised, with a prognosis of 12.4 per cent. *Corpus uteri.*—At the Memorial Hospital these cases are treated first by a diagnostic curettage and radium application followed by a full course of deep x-ray. Six weeks later an abdominal hysterectomy is performed. Often very little viable cancer is found in the uterus when it is removed. In patients who are poor operative risks no operation is performed, but a second curettage, 12 to 16 weeks after the first, is done, and if any viable tissue is obtained, a second dose of radium is given. *Ovary.* — Following laparotomy with removal of all or as much as possible of the tumour, a course of deep x-ray is advised in 4 to 8 weeks. This should be repeated in 2 to 3 months' time. *Cervix.*—Here radiation is generally accepted ts the method of treatment. Prognosis depends mainly on early diagnosis, but also on the characteristics of the cells, some being more radium resistant than others. In advanced cases Dr. Healy recommends a preliminary course of deep x-ray and vaginal douches to clean up the growth; then the radium applications, and 8 to 12 weeks later a second series of x-ray. The x-ray is given not with the hope of destroying glandular metastases, but rather to bring about changes in the connective tissue which help to interfere with the activity of the cancer cells and to kill cells lying in the tissue spaces and in the perivascular lymphatics. ELEANOR PERCIVAL

Pædiatrics

Vitamine A Deficiency in Infants. Blackfan, K. D. and Wolbach, S. B., *J. of Pædiat.*, 1933, **3**: 679.

A clinical and pathological study of 13 infants suffering from vitamine A deficiency is presented. Six cases were diagnosed by the presence of eye signs. In the seven others the diagnosis was established histologically at necropsy.

Pathologically the primary consequences of this deficiency are a specific starvation of epithelium, resulting in atrophy and finally by replacement with stratified keratinizing epithelium arising from focal proliferation of basal cells. In infants the commonest sites are the trachea and bronchi and later the renal pelvis. In the authors' opinion the important predisposing factors are the respiratory infections so commonly found in A deficiency and the loss of protective powers of the epithelium due to diminished or absent mucous secretions and loss of ciliary motion. This is regarded as the specific effect. Secondary changes observed were: (1) loss of weight, due largely to loss of fat in all storage depots, but also to muscle and organ atrophy; (2) anæmia; (3) cessation of growth of bones; (4) degenerative changes in muscles, and (5) lymphoid hypoplasia.

The 6 patients showing keratomalacia were found to have had inadequate vitamine A in their diet. Such an inadequacy was not present in the diets of the 7 whose condition was only recognized by histological changes. It is suggested that these changes are the result of grave metabolic disturbances interfering with the proper absorption storage and utilization of vitamine A or its precursor.

Vitamine A deficiency, it is maintained, is not altogether infrequent and should be suspected without regard to the absence of eye signs. Diagnostic criteria by which the disease may be diagnosed at an early stage are: (1) analysis of the dietary history; (2) consideration of all morbid processes interfering with fat utilization, such as vomiting, diarrhœa, chronic infection and diseases of the liver, gall bladder and pancreas; (3) the appearance of night blindness and xerosis; (4) the demonstration of keratinized cells in the scrapings from the cornea, nose and mouth and in the secretions of the trachea, bronchi, kidneys and vagina in suspected cases. ALAN ROSS

Urology

Cryptorchidism: Treatment and Results in 100 Cases. Counsellor, V. S., *J. of Urol.*, 1933, **30**: 327.

It is estimated that the testes are in normal position at birth in 90 per cent of infants. In many of the remainder descent takes place shortly after birth, and in some this may not

take place for one year. If the anomaly persists beyond this time the chances of descent are very remote.

Failure of descent has aroused considerable controversy as to the fundamental causes. Fetal peritonitis, producing obstructing bands of connective tissue around the spermatic vessels, is an explanation that has many supporters. It is pointed out that one frequently finds large numbers of fibrous bands along the cord and that by division of these much length can be added to the cord. In fact, this is the method commonly employed and familiar to all surgeons who have operated on these cases.

From a scientific point of view it is necessary to correct the defect before puberty, in order to prevent atrophy of the testis and to preserve the spermatogenic function. There are also other reasons; *e.g.*, cryptorchidism is usually associated with hernia; it may be painful; there may be strangulation or malignant change. The recent work of Moore has shown that it is only in the scrotum that the seminiferous tubules develop normally and produce mature spermatozoa. Moore showed that the scrotum acts as a heat-regulatory apparatus for the testes, that the temperature of the scrotum is lower than that of the peritoneal cavity, and that it varies as does the external temperature. Further, he showed that by raising the external temperature of the scrotum with hot pads degeneration similar to that seen in the intraperitoneal testis could be produced, and that by varying either the temperature or the time of application any degree of degeneration desired could be produced at will. This has shown us that not only should the testis be placed in the scrotum before puberty, but that it should hang free in the dependent position, since it is only here that it is subjected to the normal movements of contraction and relaxation resulting from thermal changes of the scrotum.

In attempting orchidopexy of any type the following principles, as laid down by Bevan, are of utmost importance: (1) division of the vaginal process below the internal ring; (2) separating the cord carefully from the peritoneum; (3) stripping the vaginal process upward and tying as in an inguinal hernia; (4) placing the testis in the scrotum and holding it there by a purse-string suture around the neck of the scrotum; (5) repair of the associated hernia. Since the scrotum is often rudimentary in these cases, and there is a tendency for the cord to retract, modifications have been developed whereby the testis is fixed to some mechanical device or to the fascia lata of the thigh. The Torek operation is the most important modification of this type, and the writer used it in 20 cases of this series with excellent results. The second stage, consisting of division of the thigh attachment, is usually performed 6 weeks after the first.

In cases in which it is not possible to obtain enough length after all attempts the vas is divided to prevent ascending infection, and the testis replaced in the abdomen. This was necessary in 7 cases. Orchidectomy was performed in 26 cases; these were mostly all in older patients who had marked atrophy, and one had cystic degeneration of the testis. The remaining cases were operated upon according to the Bevan technique, and, generally-speaking, the results in this group were inferior to those obtained with the Torek operation. N. E. BERRY

Ophthalmology

Retrobulbar Neuritis and Disease of the Nasal Accessory Sinuses. Benedict, W. L., *Arch. of Ophth.*, 1933, **9**: 893.

The toxic effect on vision and the ultimate change in the nerve that may be caused by such substances as alcohol, nicotine, lead, quinine, arsenic and thallium, are well known. Much has also been said of the effect of endogenous toxines associated with acute contagious diseases, influenza, tuberculosis, syphilis and intestinal toxæmia, and particularly disease of the paranasal sinuses. The typical syndrome of retrobulbar neuritis is not often missed. It consists of lowered visual acuity, some form of scotoma in the visual field, usually central, and a nerve-head of normal appearance. It is essential to obtain a careful history of the onset and course of visual disturbances. Loss of vision may be sudden or gradual. In cases caused by inflammation it usually is acute. Within a few hours, often overnight, the vision of one eye may be completely destroyed. In many cases perception of moving objects returns within a day or two. In mild cases the loss of vision may extend slowly for several days, varying in extent and amount but with predominance in the central or centrocæcal area. The simultaneous occurrence of symptoms in both eyes is rare. Recovery in acute cases is usually rapid, beginning a few days after the onset. Improvement continues for from four to eight days, when progress seems to be arrested. In many cases of acute onset and in cases of mild intensity central vision may remain almost stationary for days and even weeks. Pain is not a common symptom in retrobulbar neuritis. The characteristic field defect is a round central scotoma from five to fifteen degrees in size. Peripheral scotomas appear and disappear, and anopsia changes in amount, although rarely in position. The most constant feature is the central scotoma. The effects on the optic nerve of disease of the nasal accessory sinuses are not established. Traquair stated: "In Edinburgh we have come to the conclusion that rhinogenic retrobulbar neuritis is a very rare condition."

The etiology of 225 cases of retrobulbar neuritis at the Mayo Clinic was determined as

follows: multiple sclerosis in 155 cases; pernicious anæmia and nicotine in 14; diabetes in 14; alcohol and tobacco in 28; syphilis in 2; congenital amblyopia in 4; familial causes, sinus diseases, post-partum hæmorrhage, 1 each; plumbism in 2; and indeterminate causes in 3.

The treatment of retrobulbar neuritis, when the etiology is definitely known, consists in the removal of the cause, and the employment of such measures as may be expected to restore function to the nerves as quickly as possible.

S. HANFORD MCKEE

The Proper Time for Operation in Strabismus. Dunnington, J. H., *Arch. of Ophth.*, 1933, **10**: 439.

At what age should patients with strabismus be operated upon? The answer is not so simple as the questioner often thinks. The following should be known before a decision to operate can be arrived at. First, a complete diagnosis of the motor anomaly is essential. Such a study should include an accurate measurement of the amount of the deviation at 6 metres and 33 cm. One must know the amount of the deviation in each of the different directions of gaze. Notation on the presence or absence of diplopia or binocular vision should be made. Careful measurement of the deviation, both with and without the correction, is essential. The value of all non-operative measures should be weighed in each case, and operation advised only when one is convinced that in surgical intervention lies the only relief. In rare instances, a convergent squint spontaneously disappears during the growing period. This occurs as a result of developmental changes in the structure of the orbit. Secondary muscular changes occur in squints of long standing. Over-active muscles become rigid, while the under-active ones become stretched and weakened. The presence of a disfiguring squint is a great handicap to children from both a physical and mental standpoint. Removal of the cosmetic blemish prior to school age rids them of a terrific handicap and is the strongest reason of all for early operation. The author is positive that no arbitrary age limit should be adopted. Let each case be decided on its own merits.

S. HANFORD MCKEE

Neurology and Psychiatry

The Propriety of Diagnostic Lumbar Puncture in Intracranial Hypertension. Schaller, W. F., *J. Neurol. & Psychopathol.*, 1933, **14**: 54.

At the outset the author takes the stand that the not infrequent autopsy finding of cerebellar herniation into the foramen magnum is not due to any *sudden* alteration of intracranial pressure but more probably to the gradual distortion of cerebral œdema.

He presents experimental evidence of a convincing type. After injection of the subarachnoid space in the cadaver with a radio-opaque substance, experimental alterations of the intracranial pressure, by raising it to high levels and then suddenly releasing the pressure, produced no movement in the contents of the posterior fossa. In a second series of experiments, pairs of dogs were anæsthetized and their intracranial pressure raised to 750 mm. H.O., that of dog A for four hours, that of dog B for half-an-hour, and then suddenly reduced. It was found that the evidence of cerebral œdema was more marked in B than A.

To reinforce the experimental evidence, clinical data are presented on 103 unselected lumbar punctures on cases of increased intracranial pressure. In only 11 of the 103 cases were any sequelæ noted and there were but 4 deaths in the series. In two of the fatal cases the technique of puncture was extremely faulty—no pressure readings taken, etc., and in both the others, no herniation could be made out.

Schaller's conclusions are that there is no proof, experimental or clinical, to show that reduction in intracranial pressure produces herniation of posterior fossa contents, the common cause of such herniation being cerebral œdema, which, admittedly, may follow excessive removal of spinal fluid. It is his contention that properly performed diagnostic puncture in cases of increased intracranial pressure is an entirely justifiable procedure, attended by a minimum of risk and infinitely preferable to the alternative of ventricular puncture.

G. N. PATERSON-SMYTH

Injuries of the Spinal Cord and its Roots Following Dislocation of the Cervical Spine. Towne, E. B., *Surg., Gyn. & Obst.*, 1933, **57**: 783.

Injury to the cervical spine may be suspected from the history of the accident, the position of the head, the patient's disinclination to move the neck because of pain, and tenderness on palpation. Lateral x-ray films will usually establish the diagnosis. In an early case of partial, or even complete, motor and sensory paralysis it is impossible to know how much of the paralysis is permanent, because due to laceration, or how much will clear up when the hæmorrhage and œdema have disappeared. A complete anatomical interruption cannot be diagnosed for several weeks.

Reduction and fixation of the dislocation offers the best chance for restoration of function in the spine, the nerve roots, and the spinal cord in so far as the injury to the cord is not due to actual laceration. Laminectomy can do no good in these cases and may do harm. Transportation of these patients before reduction and fixation is extremely dangerous. Reduction is accomplished by Taylor's method, and is followed by complete immobilization in a plaster cuirass. A simplified method is described whereby these procedures may be executed without the aid of

a Hawley table and a skilled assistant. A plaster girdle is first applied to the chest and abdomen, allowed to dry, following which the dislocation is reduced and additional plaster applied to head, neck and shoulders. FRANK A. TURNBULL

Dermatology

Nickel Dermatitis from Spectacle Frames and Wrist Watch. Fox. H., *J. Am. M. Ass.*, 1933, **101**: 1066.

The patient, whose case is reported, had worn tortoise shell spectacles for years, but changed to "white gold" rims four and one-half months before the eruption appeared. He first noticed that the rims of the "white gold" spectacles were beginning to tarnish and a week later the eruption appeared on the skin of the face in contact with the metal. The eruption disappeared three or four weeks after he discontinued wearing the glasses. The evidence condemning "white gold" as being the factor producing the dermatitis was strengthened when the patient developed an eruption on his wrist following the wearing of a nickel-plated wrist watch. As "white gold" is an alloy containing nickel, it seems reasonable to assume that this metal was the cause of the dermatitis. NORMAN M. WRONG

Resorcin Anal Dermatitis due to Resorcin in Anusol Suppositories. Mitchell J. H., *J. Am. M. Ass.*, 1933, **101**: 1067.

Resorcin is a drug which is used very extensively for external application, but eruptions due to it are rare. Two cases are reported, and in both a severe dermatitis developed after the use of Anusol suppositories. The author conducted patch tests with Anusol, resorcin and its isomers. It was found that the patients were sensitive to all of these substances. From the clinical findings and the clinical and laboratory tests performed, the author has established the fact that these two patients, were suffering from a dermatitis due to the resorcin in Anusol suppositories. NORMAN M. WRONG

Sarcomatoid Fibroma of the Skin. McMaster, P. E., *Ann. of Surg.*, 1934, **99**: 338.

The characteristics of this skin tumour are as follows. It has a single origin, usually on the trunk; it is a firm, painless growth, nodular in the early stage, but later protruding in the form of pedunculated masses, growing away from the body, freely movable over the fascia; a bluish-red discoloration of the skin; it is histologically similar to fibrosarcoma, but invades only adipose tissue, never metastasizing, but recurs if inadequately excised.

The exact etiology is unknown. Trauma was noted in 8 cases. Heredity played no part. The average age of onset was 30. Males and females were about equally represented. The duration ranged from 1 to 60 years. General health was excellent.

A small painless firm nodule in the skin is first noticed, usually on the abdomen. No cases have been reported with lesions on the head or below the thighs. As the nodule enlarges a plaque is formed, often by the union of new nodules. Nodular excrescences may develop on the plaque. The characteristic feature is the outward growth. Spontaneous regression in size of some of the nodules has been noted. The overlying skin, normal in colour at first, gradually becomes discoloured. The mechanical rubbing of the clothes, or other trauma, may cause ulceration.

The author itemizes 38 cases from the literature, and adds one. The pathological features which are characteristic are discussed. Sarcomatoid skin fibroma is suggested as a descriptive and not misleading name. STUART GORDON

Therapeutics

A New Treatment for Cancer. Magian, A. C.. *J. State Med.*, 1933, **41**: 657.

Cancer has been treated, apart from operation, radium and x-rays, by the lead treatment of Blair Bell, the removal of the ovaries, as advocated by Beatson, the injection of cuprase, and the empirical use of various drugs and chemicals without any attempt at explanation of the why and wherefore. No one so far has used human placenta and ovary. The author's treatment consists in the injection of fresh human placenta and ovary, plus certain special sera and assisted by repeated blood transfusions. This treatment may be used alone in certain cases, but is of most service when combined with present-day procedures, and to prevent recurrences. The treatment improves the patient's chances of cure by about 25 per cent in cases where operation and radium are being, or have just been, employed.

The gland tissue used must be absolutely fresh and sterile. Placental tissue is most active when obtained by Cæsarean section. Ovarian tissue is obtained from patients who for reasons of benefit to themselves require the removal of healthy ovary. It is important to make certain, of course, that the donors of the placenta and ovary are healthy, and not suffering from syphilis, tubercle, or other communicable disease. The placenta is cleared of membranes and cord; it is finely minced and pounded up with glycerine in saline solution. The thick solution is squeezed out, filtered through muslin, and then passed under pressure through coarse, medium and fine filter candles. When ready the solution is bottled in sterile vessels and kept on ice. It should be used within a week, and before use

proved to be sterile. Ovarian extract is prepared in the same way. No preservative is added and no heat must be employed. The fresh extracts are used as intramuscular injections, generally 1 to 5 c.c., intramuscularly, once or twice a week. The exact amount of placenta and ovary to be injected cannot be definitely stated. It varies with the case, and this variation is determined at present by one's own personal experience. The author injects as much as he can, but prefers to proceed slowly. If an overdose has been given, of if the solution has been kept too long, there is a rise of temperature (up to 103°), rigors and a feeling of severe discomfort. Tolerance is never certain, and after several injections without the least after-trouble a sudden reaction of a violent nature may follow the injection of a moderate dose of a perfectly sterile and perfectly fresh extract. In many cases mild pyrexia and general discomfort may be found to occur within twenty-four hours. This should be treated with a purge and rest in bed.

The ovarian and placental tissue must be human and not animal tissue, the latter being of no use whatever. The extracts may be used with equally good results in either males or females. In cases which do not react well to ovary and placenta, a serum derived from the mixed sera of the bloods of several cancer patients mixed together is used, and in cases complicated by a good deal of sepsis injections of anti-streptococcus serum are sometimes necessary and always of advantage. Repeated blood transfusions after the removal of the growth have a very important and far-reaching effect, and are employed as extensively as possible in all advanced cases.

Out of 250 cases taken at fairly early stages of the disease 75 per cent have been cured, *i.e.*, they have been free from recurrence for a minimum period of five years. In these cases surgery, radiology and injections of placenta and ovary were used. Although any other possible beneficial procedure was always used where it was likely to help, nevertheless the high percentage of successful results is due to the regular and free injection of the placental and ovarian extracts. In advanced and inoperable cancers the injections produce considerable benefit by lessening pain, reducing hæmorrhage, and improving the general health.

In cancer of the œsophagus or other narrow channels the injections are not always beneficial, owing to fibrous tissue formation and all such cases must be kept in bed under the most careful supervision, lest the new formation of cicatricial tissue without much definite warning should close the canal completely. Treatment may need to be continued over months or even years, and all cases need constant watching. GUY H. FISK

Hygiene and Public Health

The Influence of Sanatorium Treatment on the Death Rate from Tuberculosis. Macklin, M. T., *Trans. Am. Hosp. Ass.*, 1934.

It is a well known fact that the death rate from tuberculosis was declining even before sanatorium treatment for this disease was begun. Therefore some question has been raised concerning the value of sanatorium treatment, and the advisability of its expense to the public, which contributes in large measure to the upkeep of these institutions.

The present study is concerned with the death rates from tuberculosis in the various provinces of Canada, some of which differ widely from each other in the adequacy of their sanatorium accommodation for tuberculous patients. It shows rather definitely that there is a decided relation between the two factors of death rate and sanatorium accommodation. The poorer the facilities for the care of the tuberculous patients, the higher the death rate from the disease. The sanatoria not only benefit the patients who are in them, but act as quarantining stations as well, preventing the spread of the infection to the remainder of the population. Thus they contribute to the lowering of the death rate of the tuberculous patient through treatments, and prevent the healthy persons outside their walls from becoming ill. There seems to be every justification for the expense of the sanatoria, inasmuch as they pay good dividends in public health. A number of tables and graphs, derived from the vital statistics of Canada, are given.

A. G. NICHOLLS

Pathology and Experimental Medicine

Food and Goitre. McCarrison, R., *Brit. M. J.*, 1933, **2**: 671.

This paper forms a brilliant survey of the complex inter-relations between goitre and various metabolic and nutritional factors. Many interesting facts confirmed by animal experimentation are here presented. It is noted that while a meat diet is harmful in hyperthyroid states, the casein of milk is definitely beneficial. There has been proved a definite antagonism between thyroid gland activity and fat metabolism. The thyroid seems to have a direct stimulating katabolic effect on the calcium deposits of the bones. The administration of inorganic phosphates intensifies the effects of thyroid administration, while that of calcium diminishes thyroid action. The thyroid certainly controls the utilization of iodine in the body. It is also concerned with the metabolism of water, thyroid administration diminishing the capacity of the tissues to hold water, while thyroid deprivation augments it.

No other part of the body, with the possible exception of the thymus and adrenals, is more

sensitive to food conditions than is the thyroid. This sensitivity is greatest early in life. Food may either impose upon the thyroid a burden of work greater than it can bear without undergoing hypertrophy and subsequent strain fibrosis, or, because of the food's improper constitution, the physiological efficiency of the gland may become impaired. In these circumstances the thyroid is less able to withstand the attacks of toxic agents. This aspect of the genesis of goitre—the nutrition of the gland itself—is often overlooked. Certain experiments submitted by the author show clearly that goitre may develop in experimental animals despite the adequate ingestion of iodine as potassium iodide. They also show clearly that vitamin deficiency has an important relationship to goitre. It is found that unbalanced diets lead to goitre; the imbalance may be in the direction of excess or of deficiency. Protein deficiency tends to goitre—excess protein to glands smaller than average. Excess fat is favourable to goitre, but goitre is prevented in such cases by the adequate ingestion of iodine. Butter added to diets deficient in fats and fat-soluble vitamins counteracts any tendency to goitre induced by such a diet, but if added to an already complete diet it has a definite goitrogenic action. Excess calcium is definitely goitrogenic also, but is counteracted by iodine; excess iodine itself may cause a 50 per cent increase in the size of the gland and this is counteracted by adding calcium to the diet. There are certain identified substances in plants of the cabbage family which are definitely goitrogenic.

It has been found that certain types of oxygen deficiency, and deficiency of either vitamin A, B or C may lead to goitre. Iodine deficiency is of course of great importance, but "it is not the whole orchestra as some would have us believe". McCarrison points out that there is no such thing as a "completely iodine-free diet". He states merely that "a low intake of iodine may, in certain conditions of diet and of hygiene, predispose to the occurrence of goitre and may even be a determining cause of its endemicity". Iodine is a stimulant of the thyroid, both of its growth and of its activity; therefore, "It is difficult to credit a view which attributes to iodine a direct hyperplasia-producing action on the thyroid". On the other hand, in all conditions giving rise to an unusual demand on the part of the body for thyroid products the additional provision of iodine in physiological amounts makes it easier for the thyroid to supply them. Iodine will prevent all goitres of the work-hypertrophy type, those caused by insanitary conditions, excessive ingestion of fats, or by the unidentified substance contained in certain vegetable foods; it will not prevent and may favour the occurrence of goitres arising in consequence of malnutrition and physiological inefficiency of the gland. Finally, "It is certain that the more perfect the constitution of the diet, the more perfect is the thyroid gland, both as to its size and as to its action."

W. FORD CONNELL

Cultivation of Sporozoa from Flexner-Jobling Tumours. Newiadomski, M. M., *Le Cancer*, 1933, **10**: 31.

The author begins by pointing out that protozoological methods are neglected in the investigation of human cancer cases, so that protistic ingredients of tumours are necessarily missed. The atypical cells are accounted for in other ways than the correct one through not being studied by suitable methods. He therefore describes a method of demonstrating organisms of the class of sporozoa from mouse tumours and rat tumours. The juice of the tumour is taken up with aseptic precautions by a Pasteur pipette, and planted upon asparagin agar. The first 48 hours' incubation is at 22° C. Van Delden medium was also successfully used. Chromidial cysts formed within 6 months.

He traces out phases of development which indicate that the organism is a schizogregarine (monosporea), but does not decide whether it is an exciting agent for the neoplasms, or is only a vector. Schizogony, formation of rosettes, gamete formation, sporozoite formation are described. The same bodies can be seen in tumour smears when studied by the same cytological technique (Schaudinn, Giemsa, Heidenhain) especially where the tumour is 1 to 1½ months old. Where the growth is transferred intraperitoneally, and the exudate incubated at 28 to 37° for from 1 to 6 months, the multiplication of various forms of the gregarine is easily followed.

O. C. GRUNER

Does the Tomato Cause Sarcoma in the Rat? Nicod, J. L., de Coulon, A. and Ugo, A., *Bull. de l'Assoc. Française pour l'Etude du Cancer*, 1933, **22**: 392.

A paper by Ch. Oberling, M. Guerin and M. Zahnder on the same subject immediately follows the above. See pp. 401-413. The work already published on this subject since the publication of Bellowes, from Askanazy's laboratory is reviewed and discussed. The authors conclude that the growths must have been foreign-body granulomata, for in the few instances in which nodules appeared, in their experiments nothing but granulomatous tissue appeared. In one series of 8 rats only 1 showed nodules; in the other series (20 rats, 10 mice, 4 rabbits) no tumours in any, but sclerotic inflammatory nodules in some rats. One rabbit showed milk-spots on the peritoneum.

[In these papers, and in all those reviewed by the first named workers, there is no effort at a critical analysis of the principles involved in the original publication. The bacteriology of the tomato is ignored, and institution of mere feeding experiments with a very familiar article of food might be deemed *ipso facto* superfluous. Reviewer].

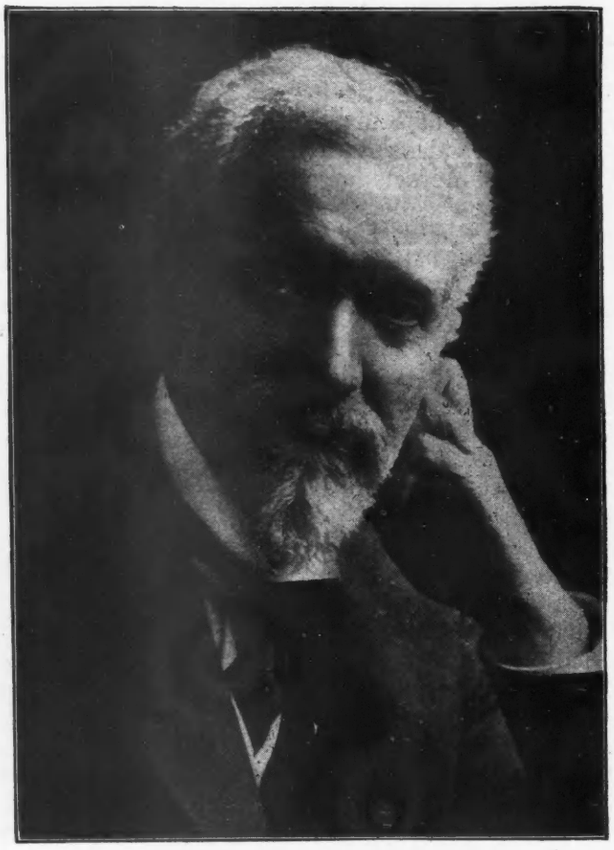
O. C. GRUNER

Obituaries

Archibald Byron Macallum, M.A., M.D., Ph.D., Hon. D.Sc., LL.D., F.R.S., F.R.S.C.

Dr. Archibald Byron Macallum died at his home in London, Ont., early on the morning of April 5th, after a year's illness. In Dr. Macallum Canada loses one of the most distinguished scientists she ever produced, a man outstanding all over the world in the field of biochemistry. His great achievements were never spectacular, but among the scientists of the nations he was recognized as a leader.

Dr. Macallum was born in 1858 on a farm in Westminster township, Ont., the son of Alexander Macallum, who came to this country from Scotland in 1830 and pioneered in what was then bush country near London. Owing to the fact that vital statistics were not systematically recorded until the year of Confederation (1867) the exact date of his birth is unknown. He had 6 sisters and 5 brothers, two of whom became doctors. He was educated in the township schools and in the high schools of London. He obtained a first-class teacher's certificate and went back to Westminster township to take a rural school, in order to earn money to put himself through university. Even as a boy in his 'teens he was ambitious to obtain a good education.



Archibald Byron Macallum

Attending the University of Toronto, he graduated with an arts degree in 1880 and won the silver medal for natural sciences, demonstrating early the tremendous ability in the field of research which was later to secure him a lasting international reputation. He then went into teaching high school in the town of Cornwall. There he met a young lawyer, James Whitney, and established a friendship that lasted throughout the lifetime of the man who later was to become Sir James Whitney, for a long time Prime Minister of Ontario. Much of the educational legislation that was passed during the Whitney régime at Queen's Park was influenced by the Premier's friendship with Dr. Macallum, and the cause of higher education was immeasurably benefited by this happy association.

From 1880 to 1883, while he was engaged in high school teaching, he was collaborating with the late Prof. R. Ramsay Wright, Prof. J. P. McMurrich, and the late Dr. Thomas MacKenzie, of Toronto, on the study of the anatomy and physiology of the catfish. He discovered that the pancreas, which was hitherto believed to be non-existent in this fish, was embedded in the liver.

In 1883 Dr. Macallum returned to the University of Toronto, this time as a member of the faculty and Lecturer in Biology. He obtained his medical degree in 1889 and his master of arts degree in 1889 and his master of arts degree in the same year. A man of wide culture, he was a voracious reader and never confined his active mind to one field of study. He obtained his degree of doctor of philosophy from Johns Hopkins University in 1888. From 1890 to 1908 he was Professor of Physiology at the University of Toronto, and from 1908-16 Professor of Biochemistry in the same institution, where he broke new ground through his intelligent research in his field. His work might be said to be in the determination of fundamental principles, and the general advancement of science, but particularly with relation to the chemistry of blood and tissues.

Ordinarily a list of degrees may not be a true measure of a man's life work, but in the case of Dr. Macallum they were all deserved through hard work and steady application. He was a Fellow of the Philadelphia College of Physicians; a Fellow of the Royal Society of Canada; local secretary of the British Association for the Advancement of Science in 1897. He was the first University of Toronto graduate to be elected to the Royal Society of England (1906); a member of the Royal Philosophical Society of Glasgow. He held honorary degrees from Aberdeen, McGill, Toronto, Trinity College, Dublin, and Yale.

He was appointed Herter Lecturer in New York in 1918, and Hatfield Lecturer before the College of Physicians in Philadephia in 1917.

In 1917, at the time of the Union Government, when Sir Robert Borden was Prime Minister, the late Hume Cronyn was member of Parliament. It was Mr. Cronyn who first urged the necessity of research on a national scale, and a special committee of Parliament was appointed, which later brought in a series of recommendations, one of which was that a national research council should be established. It was natural, in view of his record, that Dr. Macallum should be appointed the first chairman. He served in this capacity for three years, and he must receive a large measure of the credit for the success which the foundation has since received. He established it solidly on sound scientific principles, and his work in this connection will live for generations after his death.

To the advancement of general education, as we have said, he contributed through his association with

Sir James Whitney. He had much to do with the framing of the organization bill of the University of Toronto which was put through the Legislature in 1905. This was a revision of the charter, and there was much opposition to it at the time. In those days the Government was not financially interested in higher education as it is today. The university was almost paying its way, the deficits running around $30,000 a year. However, expansion was required and governmental financial assistance was necessary, and Dr. Macallum's efforts bore fruit in this direction.

In 1897 Dr. Macallum was chairman of the local committee of the British Science Association during its meeting in Toronto. He was also the representative of the Ontario Government on the Board of Trustees of the Toronto General Hospital from 1907 to 1913.

In 1920 Dr. Macallum went to McGill University as Professor of Biochemistry, retiring from active work in 1928. His ability and international reputation were recognized in 1921 by the Rockefeller Foundation when he was sent as visiting professor to the Peking Union College, where he rendered distinguished service. In 1906 he visited South Africa, where he attended the convention of that year of the British Association for the Advancement of Science. He attended in 1932 the International Physiological Congress in Rome. Not satisfied with listening merely to papers and lectures, he embarked on a research expedition of his own down the Mediterranean coast.

During the past forty-five years his studies covered a large number of subjects. In 1888 he reported the discovery of the origin of hæmoglobin from the nuclear chromatin in embryonic red cells. In 1892 he demonstrated the presence of "masked" iron in the chromatin of every cell, and proposed the generalization that as hæmoglobin is derived from chromatin the latter must have respiratory powers. Between 1898 and 1908 he demonstrated by microchemical methods the exact localization in cells, animal and vegetable, of calcium, potassium, chlorine and phosphoric acid, and presented the results he had obtained in communications to the Royal Society of London. This was followed by a demonstration of the relation of potassium to adsorption in the cell. After this, Professor Macallum carried out a very interesting investigation on the relation between the inorganic salts of sea water and those in the tissues of jelly fishes, which led to a formulation of the origin of the salts in the blood plasma of vertebrates. In the lower marine invertebrates, which have a circulation not closed off from the sea water, the circulatory fluid is sea water. In those invertebrates with a closed circulation, which have been denizens of the sea since the Silurian period, the circulatory fluid is practically sea water of today. In vertebrates the inorganic salts of the blood are in a concentration less than one-third of the concentration of those same elements of the sea water of today, but by ranging the concentration of the sodium, potassium, calcium and magnesium in ratios, with sodium as 100, there was revealed a similarity to sea water, with the same elements, except in regard to magnesium. From this followed the generalization that the salts of the blood plasma in their concentration are those of the sea water of the Cambrian or Silurian period. In that age the concentration of the salts in the sea must have been less than one-third of what it is in the ocean of the present day, and also the proportion of magnesium was greatly less than it is now. The factor in maintaining this ancient ocean concentration in the blood plasma is to be found in the kidneys of vertebrates, which rigidly control the inorganic composition of the blood plasma. The kidneys have rendered it possible for vertebrates to change their environment without changing the inorganic composition of their blood, whereas amongst invertebrates such a maintenance of uniformity in the blood plasma is not possible, and, consequently, a high degree of evolution amongst invertebrates is possible. This led to a study of the inorganic composition of the living cell, and it was found that the proportions of the elements, sodium, potassium, calcium and magnesium, are utterly unlike those found in the blood plasma. Hence the conclusion that the organic composition of the cell harks back to a more remote geological age, to a time when the organism was unicellular, and when there diffused into it the salts of its environment. On the other hand the animal cell represents in its organic composition the sea water of a period much earlier than the Cambrian. Therefore it may be stated that in the blood plasma we meet with sea water of the Cambrian period and in the cell itself a sea water of a date many millions of years earlier.

After his retirement from McGill, with the title of Emeritus Professor of Biochemistry, Dr. Macallum lived in London, Ont., but his days were never idle. He had an office in the Medical School building which he visited daily. There he consulted members of the staff and helped students with difficult research problems. In such high esteem was his opinion held that he was constantly being referred to. At the same time he took a keen and intelligent interest in current events, at home and abroad. He was a student of the body politic as well as a student of the human body. His years of retirement did not dull his interest in life; rather, they sharpened it if anything.

Dr. Macallum's one physical recreation was golf. He was an ardent and enthusiastic golfer, back in the days when men in plus-fours, swinging their awkward-looking clubs, were laughed at. A member of the London Hunt and Country Club, he played golf until the last few months of his life. He was a member also of the University Club of Montreal and the York Club, Toronto.

While never in public life himself, devoting his entire time to research, he had many close friendships with distinguished men besides Borden and Whitney, the late Sir George Foster, Hon. H. H. Stevens, now Minister of Trade and Commerce, and Rt. Hon. R. B. Bennett.

His old friend, Prof. J. P. McMurrich, gives us the following picture of a strong character and a remarkable personality.

"Professor Macallum was tall, lank, rugged and somewhat 'dour', of the Highland Scot type and with all the Scot's pertinacity. To whatever interested him he gave serious consideration, decided upon what seemed best, and then fought for that uncompromisingly and with all his energies. To his opponents he was anathema, but to his friends he revealed himself as a good companion, fond of congenial company, fond of good cheer, fond of a good story well told, fond of a game of golf, and fond of good poetry, for which he had a most retentive memory. One can visualize him testing the acoustic properties of an old Greek theatre, standing upon the stage and declaiming Matthew Arnold to his companions opposite him on the topmost tier of the amphitheatre. With congenial companions his dourness vanished."

Dr. Macallum is survived by his widow and three sons, Dr. A. Bruce Macallum, Dean of the Medical School of the University of Western Ontario; E. N., president of the Synthetic Drug Company, of Toronto, and A. D., research chemist in the DuPont plant at Niagara Falls, Ont.

Dr. William Walter Beattie, of Montreal, was instantly killed in a motor accident near Biggleswade, Bedfordshire, England, on April 13, 1934. His motorcar mounted the footpath, jumped the ditch and a hedge, and stopped upside down, while Dr. Beattie was thrown into the air, his neck being broken as he fell.

Dr. Beattie graduated from the Faculty of Medicine of McGill University in 1920, after completing his studies in the Faculty of Arts. One year after graduation he

was added to the medical faculty staff as assistant curator to the medical museum. In 1926 he was appointed lecturer in bacteriology. A brilliant student, he continued his studies both in Montreal and in New York City. Last fall he went over to London to do special work and was studying at Queen Charlotte's Hospital.

Dr. Beattie was a native of Montreal, and was forty years of age. His father, the late John Beattie, came from Scotland. The family survivors are his mother, Mrs. John Beattie; two brothers, Rev. D. Beattie, who is minister of a parish in Scotland, and James R. Beattie, and one sister, Miss Jessie Beattie, both the last of Montreal.

Dr. Joseph Esdras Beaudet died on February 28, 1934, at St.-Jean Deschaillons at the age of 60. He had studied at the Quebec Seminary and Laval University where he graduated in medicine in 1898. He then practised at Notre-Dame-du-Lac for five years and finally settled in his native town for the rest of his life.

Dr. Achille Besner, of Valleyfield, coroner for the district of Beauharnois, died suddenly on February 15, 1934, from angina pectoris, at the age of 62. He took his degree in medicine at Laval University, Montreal, in 1892.

Dr. William Black died on April 3, 1934, following an attack of cerebral hæmorrhage. He was born in Bruce County, Ont., spent his boyhood at Morden, Man., and graduated from the Manitoba Medical College in 1903. During the war he served as Medical Officer with a Winnipeg regiment.

Dr. Frederick Graham Brien, of Elphinstone, Man., died on December 30, 1933, in the Winnipeg General Hospital, after a brief illness, at the age of 71 years. He was born in Lindsay, Ont., and attended school there and later the Normal School at Ottawa. He came west as a young man and was principal of schools at Birtle and Selkirk. He then took up the study of medicine and graduated in 1894 from the Manitoba Medical College. He practised at Dugald, Douglas and Winnipeg, Kerrobert, Sask., Peachland, B.C., and lastly at Elphinstone.

Studious by nature and a sound classical student, Dr. Brien bore the reputation among his friends of being one of the best-read men in the province, though his modesty and unassuming nature prevented a wider recognition of his gifts. He was a sound practitioner and a delightful companion.

Dr. Félix Cornu died in Montreal on January 29. 1934, at the age of 68. He had lived in Buckingham for about 20 years. He was a graduate of Victoria University Medical School in 1887.

Dr. Herbert Ernest Cumming died at Hereford, England, on March 20, 1934. Dr. Cumming graduated in medicine from McGill in 1913 and was one of the first to go overseas with the McGill Corps. He was a graduate also of the Vankleek Hill Canadian Institute and taught school in Ontario and Saskatchewan for a few years. While at the University he took a prominent part in its athletic activities and among other things played soccer. He belonged to the McGill Rifle Club and boxing class.

Dr. Frederick Charles Delahey, of Pembroke, Ont., died on February 8, 1934. He was born in 1870 and was a graduate of the University of Toronto (1895).

Dr. Cummins Van Norman Emory, of Hamilton, a homœopathic physician, not in practice, died on March 16, 1934, in Florida. He was born in 1850 and was a graduate of the Homœopathic Hospital College of Cleveland (1879). Dr. Emory was a former Dominion Secretary of the Royal Templars of Temperance.

Dr. L. A. Genest died at the General Hospital of Quebec on February 10, 1934, at the age of 70. He was born at St-Henri-de-Lévis. He graduated from the University of Montreal in 1892 and practised until 1903 at Sherbrooke, Que., and since then at Legal, Alta.

Dr. William Hall, the oldest resident practitioner in Saskatchewan, died at Fort Qu'Appelle December 31, 1933. He was born on May 25, 1856, in Norfolk County near Waterford, Ont., of English parentage, from Yorkshire. He was educated at Woodstock College and Queen's University and graduated in 1883. Following graduation he came west, opened a practice at Fort Qu'Appelle on June 3, 1883. The following year he married Miss Jane Webster, of London, Ont., a descendant of an old United Empire Loyalist family who moved from New York State to south-western Ontario in 1776. To them was born one child, Clayton, who afterwards graduated in arts and medicine from Toronto University, served with distinction overseas, and on returning home took up his father's practice in Fort Qu'Appelle. The year following Dr. Hall's marriage saw the North-west Rebellion. Dr. Middleton established his headquarters at Fort Qu'Appelle, and Dr. Hall gave medical care to these forces.

For many years Dr. Hall had been the oldest resident practitioner in the Province of Saskatchewan, having practised there nearly fifty years. During this period he served as physician to the Indians on various reservations. He had a very keen interest in the health of the Indians, and his personal knowledge of them was of great assistance in the recent research into the health of Indians of the Qu'Appelle Valley, reported in 1928. Dr. Hall was recognized by his confrères as an outstanding practitioner, and during his long period of medical service he continuously retained the confidence and respect of his patients. His fellow practitioners throughout the province made him a life-member of their Association in 1932. In 1932, also, the citizens of Fort Qu'Appelle and district honoured him at a gathering at which was presented an illuminated address, signed by all organizations and public bodies in the community. He took a keen interest in the public affairs of the community, and lent his support to all efforts for the welfare of the community. He served as Overseer of the Village of Fort Qu'Appelle; was appointed Honorary President of the Golf Club, Curling Club, and Great War Veterans' Association. His hale manner and kindly presence will be greatly missed by his friends, and especially by the sick, in whose service his generosity and kindness knew no end.

R. G. FERGUSON

Dr. Marion Hansford. One of the first woman doctors in Montreal, Dr. Marion Hansford, for nearly a quarter of a century school medical inspector, died suddenly recently at the Homœopathic Hospital. Stricken while at work at the Iona Avenue school, she was taken to the hospital where she died three hours later.

Before McGill University admitted women to the study of medicine, Dr. Hansford followed her course at the medical college then attached to the University of Bishop's College, graduating with an M.D. degree in the late "nineties". She was among a distinguished group of Montreal women who received their medical training there. She was in general practice for some time before engaging in special work such as being in charge of the Baby Welfare Camp on Fletcher's Field in 1919. She was a native of Lanark, Ont.

She is survived by a brother and sister in Vancouver, William and Miss Byrd Hansford. The late Col. Hansford, of Winnipeg, was a brother.

Dr. Ronald Levesque, of Montreal, died on January 14, 1934, at the age of 47, after a short illness. He was born in Montreal, graduated from Laval University,

Montreal, in 1912, and then went to Paris. He devoted himself to research.

Dr. Dick Allison Taylor died in Lethbridge, Alta., on March 27, 1934, at the age of fifty-eight years, after a considerable period of ill-health.

Graduating from McGill University in 1901, he practised for three years in his native province of Nova Scotia, coming to Alberta in 1905, where he had since resided. For many years he devoted himself to eye, ear, nose and throat work. He is survived by his widow and two children.

Dr. Charles Ernest Tran, Kamsack, Sask., died from a stroke, on March 23, 1934. While not in the best of health for some time, Dr. Tran had been actively engaged in his practice and had been attending a patient when seized.

Dr. Tran was born on January 29, 1877, at Barrie, Ont. He attended school there and was a graduate of Western University at London, 1912. He had practised at Kamsack for more than twenty years, and was mayor from 1914 to 1916, 1919, 1921, 1923, and 1926. Dr. Tran was the Independent nominee for Pelly constituency for the coming elections and served in the legislature as Progressive leader, but dropped out of politics in 1929. He was a member of both the Masonic and Odd Fellows' lodges. He was a World-War veteran, serving with the Canadian Medical Corps from 1916 until demobilization. His wife and two children, Charles Garfield, and Shirley Angeline, survive him.

Dr. John James Wade, of Coe Hill, Ont., was found dead in his office on March 24, 1934. He was apparently in his usual health the day previous. Dr. Wade was born in 1881 and graduated from Queen's University in 1906.

News Items

Great Britain

Princess Elizabeth Hospital for Children, Shadwell, London, E.I. — On February 16th, Professor Leonard Findlay presided at a lecture on "Our animal friends as patients" by Sir Frederick Hobday, C.M.G., F.R.S.E., Principal of the Royal Veterinary College and Hon. Veterinary Surgeon to the King. The address was fascinating, both in matter and delivery, interleaved with humour and pathos, and well illustrated with lantern slides and cinematograph films. Among the diseases, glanders, tuberculosis, and foot-and-mouth disease were discussed, and interesting examples were shown on the screen of artificial legs, eyes, and teeth in dogs. The lecturer spoke at some length of the modern humane method of rendering animals unconscious by electricity before slaughtering them in the usual manner. Electricity, he said, was also used for the purpose of anæsthetizing animals which have to undergo surgical operations. A vote of thanks, proposed by Dr. E. W. Goodall, and seconded by the Matron, was heartily carried by a large and enthusiastic audience.

W. R. BETT

Dr. John Cameron, formerly Professor of Anatomy at Dalhousie University, Halifax, N.S., has just published an important book, representing a lengthy and painstaking research. It is entitled "The Skeleton of British Neolithic Man"* and is dedicated to Sir Arthur Keith *veteris amicitiæ non immemor*. So far as the author could ascertain, the subject had not previously been dealt with in a systematic manner. The study is based largely upon the extensive material of prehistoric and Anglo-Saxon age which is housed in the museum of Royal College of Surgeons, London, but to some extent on remains from Minorca and Egypt. In this way it was possible to undertake a comparative study of prehistoric man in two widely separated regions of Europe. The book first describes the neolithic remains of the cranium and other bones discovered hitherto in England, and then goes into considerable detail in regard to certain individual bones and the skeleton as a whole. There are illuminating chapters on The Skeleton of British Neolithic Man, compared with Neolithic and Copper Age Skeletons from the Mediterranean Basin, and The Relation of the Prehistoric Inhabitants of Britain to the Present-day Population of that Island and of Europe in General. As there are still gaps in our knowledge regarding the anatomy of prehistoric man in Britain, the author hopes that his work may prove an incentive to further study. Professor Cameron's book is an erudite and valuable contribution to a subject which has interest not only for the pure anatomist but for the ethnologist and medical man as well.

* The Skeleton of British Neolithic Man. John Cameron, M.D., D.Sc., F.R.S.S.Edin. and Canada. Illustrated. Price 15/-. Williams and Norgate, Ltd., 28-30 Little Russell Street, London, W.C.1., 1934.

Sir Robert McCarrison.—The governing body of the Arnold Flinker and Julius Wagner-Jauregg Foundation of Vienna for research on goitre and cretinism has awarded the Foundation's prize of 2,000 Austrian shillings to Major-General Sir Robert McCarrison, I.M.S., for his researches into the etiology of goitre, upon which he presented a report at the second International Congress on Goitre, held in Bern last summer. As this prize had never before been awarded to a foreigner the statutes had to be altered for the purpose of recognizing Sir Robert McCarrison's work.

Alberta

According to the Honourable G. Hoadley, Minister of Health, the Provincial Legislative Commission on State Health Insurance does not propose to spend ten million dollars on a scheme to be put into operation under present conditions. An adequate scheme has been drafted, and how this is to be put into operation is for the Provincial Legislature to decide.

In a Bill to amend the Public Health Act, now before the Provincial Legislature, there would be a new five-year plan, under which powers of Boards of Health will be extended in order to provide "state medicine" on a modified scale. This new Bill would give the Board of Health in any city or health district which has within its area any city or town, the power to make provision for supplying medical, dental and surgical services, to any persons or class or classes of persons within the health district. In particular, this power will apply to the care of the health of school children within the school district, children of pre-school age, and expectant mothers. This Bill would empower the Board of Health to employ physicians, dentists, and nurses, and to enter into agreement with a town-school district, whereby the Board of Health undertakes the provision of the services mentioned which the School Board is empowered or is under a duty to provide by the School Act of 1931. Every agreement between a Health Board and School District is to be for a period of at least five years, and may be terminated upon a year's notice being given by any party, after a resolution passed by the party desiring to end the agreement has been ratified by the electors.

By a recent order-in-council enacted by the Provincial Government, local health authorities have been given the power to compel tuberculous persons to go to a hospital, and to remain there, even if the patient desires

to leave the institution. Local hospital authorities have stated that if this order resulted in increased admissions to hospitals the Government would be compelled to increase accommodation at the Provincial Sanatorium at Keith.

According to Government officials, the control of tuberculosis has been greatly improved in Alberta during the past few years. G. E. LEARMONTH

British Columbia

The annual Osler Lecture of the Vancouver Medical Association took place on March 7th. Dr. J. G. MacKay, the lecturer, spoke on "Psychiatry", before a very well-attended meeting, delivering an address which was of excellent character and well received.

It is announced that the provincial government will restore the per capita grant to hospitals of the province to the former rate of 70 cents a day.

A widespread epidemic of scarlet fever has broken out in and around Vancouver. So far the cases have been of a mild type, with only one or two deaths. Probably due partly to the mildness of the symptoms, and partly to prevailing financial conditions, a physician is not always called, so that the enforcement of quarantine has not been complete.

News from Victoria indicates that chiropractors have been given legal standing under their own governing body. A similar bill for drugless healers failed to pass. C. H. BASTIN

Manitoba

The regular monthly meeting of the Winnipeg Medical Society was held in the Medical College on March 16th. Dr. E. S. Moorhead, Chairman of the Special Relief Committee, presented present and future problems of the profession in Greater Winnipeg. The scientific program was composed of a paper "Modern views of chronic arthritis" by Dr. Moore McFetridge, and one on "The anatomy and physiology of the spleen" by Dr. W. A. McElmoyle.

Dr. Alexander Primrose, of Toronto, was a welcome visitor to Winnipeg on March 29th. In the morning he addressed the medical students and members of the Faculty in the Medical College. Dr. W. Harvey Smith was the host at a luncheon in his honour at the Manitoba Club, and in the evening a dinner was arranged by the University of Toronto alumni, with Mr. R. F. MacWilliams presiding.

Dr. Ross Mitchell gave an address on April 5th before the Manitoba Historical and Scientific Society on "The early doctors of Manitoba" illustrated with lantern slides.

Professor Wm. Boyd recently addressed the Medical Faculty and Medical students of the University of Pennsylvania in Philadelphia.

Dr. A. Gibson delivered the annual Lister Day address on April 5th before the professors and students of the Faculty of Medicine, University of Manitoba.
ROSS MITCHELL

New Brunswick

Dr. S. R. D. Hewitt, Medical Superintendent of the Saint John General Hospital, has been appointed an associate editor of the *Monthly Bulletin of the American Hospital Association*. Dr. Hewitt has also recently been given a charter fellowship in the American College of Hospital Administrators.

Dr. Charles McMillan, District Medical Health Officer, in the County of Saint John, reports that within the next two weeks, diphtheria immunization clinics will be in progress in the city schools. In 1929 all school children and a large number of pre-school age children were immunized. The present series of clinics will, it is anticipated, include all those who were not previously immunized.

The New Brunswick Joint Study Committee on Nurses' Education, at their recent meeting, endorsed a recommendation that training schools in mental hospitals and in tuberculosis sanatoria should be discontinued, and further that the Provincial Committee consider the advisability of staffing these hospitals with graduate nurses or with graduates and affiliates.

Dr. E. W. Lunney, Saint John, has been appointed examiner for the New Brunswick College of Physicians and Surgeons in Obstetrics, to succeed Dr. F. T. Dunlop who has resigned.

Subsequent to a joint conference between representatives of the Saint John Medical Society and the Mayor and Council of the Municipality of Saint John, it was decided that any free treatment at the Saint John General Hospital, either in the Out-Patient Department or in the wards, will in future be given only after the case has been investigated by the Municipal Relief Office, except in the case of an emergency, and even these will be subsequently investigated by the same office. This ruling has the support of the hospital commissioners.

In the report of Hon. Dr. H. I. Taylor to the New Brunswick Legislature, he mentioned a new policy of public health introduced in the province this winter. In this regard he was referring to the campaign recently concluded by the Canadian Dental Hygiene Council. The centres benefiting by this new public health effort were Saint John, Fredericton, St. Stephen, Newcastle, Woodstock, Bathurst, Campbellton and Edmundston. Twenty-two thousand school children and 650 school teachers were contacted and privileged to hear addresses on dental hygiene. Fifteen thousand children were given free and complete mouth examinations. Dr. Taylor further reports that the number of children vaccinated in the province during the last ten years was in the vicinity of 165,000. There was no small-pox during the year in New Brunswick. Diphtheria had been also receiving a lot of attention from the Department of Health in the past five years; 55,387 children had been inoculated with toxoid. Dr. Taylor drew attention to the fact that the rural portions of the province were suffering from a very great shortage of physicians.
A. STANLEY KIRKLAND

Nova Scotia

The Council of the City of Halifax has renewed a grant of $2,500 for one year towards defraying some of the expenses of the Public Health Clinic of Dalhousie University.

Miss M. G. Schurman, a graduate in Occupational Therapy, addressed a meeting of the Nova Scotia Mental Hygiene Society recently. The Society strongly favours Occupational Therapy in the Nova Scotia Hospital, and a resolution to that effect was passed and sent to the local legislature.

A resolution of much interest to the medical profession was recently passed by the Truro Presbytery. It was in favour of the following:— "That no marriage licenses be given to people without a physical examination." This proposal was discussed, and finally it was decided to refer it to the Maritime Conference in June.

Dr. E. G. Young, Professor of Biochemistry at Dalhousie University, attended the meeting of biochemists held in New York at the end of March.

N. B. DREYER

Ontario

On March 1st, the Board of Control recommended to Council that a grant of $100,000 be made to the Toronto Western Hospital to assist it in constructing an addition to take the place of Grace Hospital. The grant was made on the understanding that the addition would be built as an unemployment relief measure and that the Federal and Provincial Governments would contribute two-thirds of the cost of labour.

Tenders have been asked for the construction of a new wing of two stories to the general hospital at Clinton.

On March 15th, the new wing of the Parkwood Hospital (originally the Victoria Home for Incurables) was opened, so that the hospital now provides for over 120 patients and is now one of the most up-to-date institutions of its kind in Canada.

On April 5th, Dr. William D. Haggard, Professor of Clinical Surgery in Vanderbilt University Medical School, Nashville, Tenn., delivered the Donald C. Balfour lecture in surgery at the University of Toronto. It was the occasion of the 107th anniversary of the birth of Lord Lister.

Dr. Perry G. Goldsmith has been elected President of the American Laryngological, Rhinological and Otological Society.

J. H. ELLIOTT

A copy of a memorandum just sent us by the Honourable Dr. Robb, Minister of Health and Labour, as follows, conveys important information to the doctors of Ontario *re* medical relief.

"Dating from March 1, 1934, the following additional changes are made in connection with Medical Services:—

"(1) In addition to the one-half of $200.00 that is allowed for medical services monthly, the medical man will be allowed for prescriptions and medical supplies to the extent of 12½ per cent of the gross medical services for any month. *E.g.*, if medical services to the extent of $300.00 are given, then the medical man will receive one-half of $200.00, or $100.00 net, and in addition will receive 12½ per cent of the $300.00, or an additional amount of $37.50. Where prescriptions are written, it is understood that some provision will be made for punctual payment to the druggists. Complaints of this character will be dealt with.

"(2) Mileage will be allowed for rural work only at 10 cents per mile.

"(3) Accounts for prescriptions and medical supplies in future need not be rendered."

Saskatchewan

At the March meeting of the Regina and District Medical Society a luncheon was held in honour of Dr. Alexander Primrose, of Toronto. Dr. Primrose gave an address following the luncheon and described his recent trip through the Panama Canal. Then he outlined reasons for the medical course being six years. He said he hoped that all Canada would organize for a cancer campaign in cooperation with the British Empire Cancer League. Dr. S. E. Moore, Regina, gave a talk on "State Medicine" and Dr. R. G. Ferguson, Fort San, spoke on "Tuberculosis in nurses".

The second Post-Graduate Course will be held at Saskatoon, during the week of June 11th to June 15th. A real success is anticipated.

An amendment to the Marriage Act, requiring medical certificates of health for females, though requested by the Provincial Council of Women as qualification for application for a marriage license, will not be brought down at the present session of the legislature.

A Clinical Week was held in Regina from April 30 to May 4 inclusive. The program provided for work in the operating-rooms from 8 to 10 each morning. Sixty different subjects were discussed during the week. One day was entirely devoted to the Grey Nuns' hospital. A banquet and an entertainment were given by the Regina and District Medical Society during the week.

The Honourable Howard McConnell, Minister of Municipal Affairs introduced an amendment to the Local Improvement Districts Act, giving the minister permission to make payment to hospitals outside the province where indigent patients are given treatment. The provisions of the amending bill provide that the minister may use from the funds of the district amounts not to exceed $2.50 per day for actual treatment.

LILLIAN A. CHASE

United States

The American Association for the Study of Goitre meets at Wade Park Manor, Cleveland, O., on June 7, 8, 9, 1934. An excellent program has been arranged for. We note that Dr. Stuart Gordon, of Toronto, is down for a paper on "Clinical hyperthyroidism in the presence of a normal basal metabolic rate". Besides papers, clinics and demonstrations will be given at the University Hospitals. The Annual Dinner will be held on Friday, June 8th, at 7.30 p.m. The president is Dr. R. M. Howard.

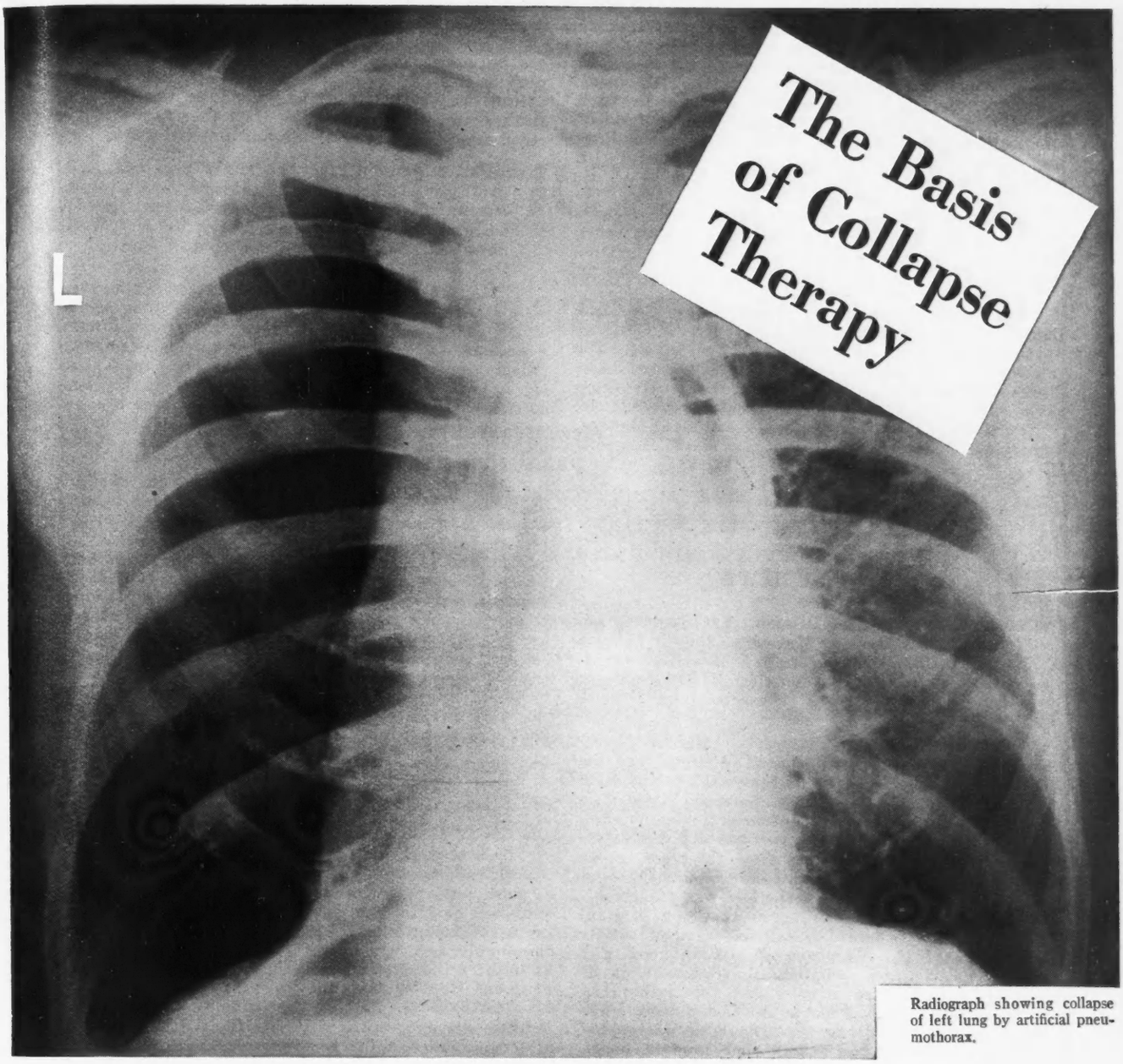
The American Academy of Tropical Medicine.—An American Academy of Tropical Medicine was formed recently by a group of leaders in the field, who met for the purpose at the National Academy of Sciences, Washington. The president of the new organization is Dr. Theobald Smith, pioneer American disease-fighter who is now on the staff of the Princeton laboratories of the Rockefeller Institute for Medical Research. Other officers are: treasurer, Prof. W. W. Cort, of the Johns Hopkins School of Hygiene and Public Health, and secretary, Dr. Earl B. McKinley, dean of the George Washington University School of Medicine.

The purposes of the Academy are to further the extension of knowledge of tropical medicine, to coordinate the work of American investigators in this field, to function as a central source of information, and to receive funds and administer them through grants in aid and in support of research.

Graduates of Toronto Medical School in Cleveland.—Graduates of the School of Medicine of the University of Toronto, residing in Cleveland, are planning a reunion of all alumni attending the meetings of the American Medical Association in that city in June, 1934. A committee consisting of W. J. Abbott, Howard Dittrick, and W. S. Duncan is in charge of arrangements. A dinner will be held at the Carter Hotel on Wednesday, June 13th, at 6.30 p.m.

General

American Association of Pathologists and Bacteriologists.—Dr. William Boyd, of Winnipeg, was elected president of the American Association of Pathologists and Bacteriologists at the annual meeting



Radiograph showing collapse of left lung by artificial pneumothorax.

The Basis of Collapse Therapy

RADIOGRAPHS are important not only in early detection of pulmonary tuberculosis, but also in determining the extent of the pulmonary region involved, and whether the lesion is of an exudative, productive, or mixed type.

X-rays have made collapse therapy of pulmonary tuberculosis possible. Whereas the stethoscope detects less than 50% of cavities, the x-ray percentage is 100. Treatment can be prompt and collapse therapy instituted immediately wherever it is applicable. Progress can be carefully watched and accurately noted.

X-ray examination by a competent radiologist should be regarded as a necessity in following through a case of tuberculosis. From the time you suspect this condition until the lesions have entirely healed, radiographs should be made regularly as a matter of routine.

RADIOGRAPHS PROVIDE DIAGNOSTIC FACTS

•If you would like to receive the free publication, "Radiography and Clinical Photography," mail the coupon below.

CANADIAN KODAK CO., LIMITED
Toronto 9, Ontario.
Gentlemen: Please send me your free publication, "Radiography and Clinical Photography," regularly.

Name.....

No. & St.....

City.....

Province.....

in Toronto. Two hundred delegates attended the sessions, including representatives of the 27th annual meeting of the American Association of Cancer Research. Dr. N. C. Foot of New York was chosen vice-president. Other officers are: Dr. F. B. Mallory, Boston, treasurer; Dr. Howard T. Karsner, Cleveland, secretary; Dr. Allen R. Moritz, Cleveland, assistant secretary.

The Fourth International Congress of Radiology will be held in Zurich, Switzerland, from July 24 to 31, 1934. The President is Prof. Dr. H. R. Sclunz and the Secretary, Dr. H. E. Walther, Zurich, Gloriastrasse 14.

The Sixth International Medical Post-Graduate Course of the Tomarkin Foundation will be held at St. Moritz, Switzerland, from August 5 to 18, 1934. The subjects to be dealt with during the course are: heart diseases, diseases of children, nutrition, balneology, gastro-enteric diseases, social medicine, and others.

Particulars may be obtained from the Secretary, Tomarkin Foundation, Rome, Italy, Via Marco Minghetti 17.

Book Reviews

The Medical Treatment of Disease. For Students and Young Practitioners of Medicine. Robert Dawson Rudolf, C.B.E., M.D., F.R.C.P., Professor of Therapeutics, University of Toronto. Fourth edition; 540 pages. Price $4.00. University of Toronto Press, 1934.

The fourth edition of Rudolf's "Medical Treatment of Disease" is a book somewhat larger than the third, but the subject matter is comprised in the same number of chapters, classified as before. While it is obvious that there are a few deletions numerous additions are noted and not a few portions are re-written. New references and quotations from the more recent works on therapeutics enrich this edition, although but three years have elapsed since the last was published.

We are quite ready to agree that the original plan of the book, where diseases are discussed under the headings of (1) diagnosis, (2) environment, (3) diet, (4) specific and symptomatic treatment, is of value, and are likewise pleased that the author has seen fit to retain it. Thus a hand-book useful for the student and the young practitioner in his everyday work is now for the fourth time brought up to date for the profession. While the text clearly reflects the teaching generally accepted, an important and valuable personal touch is added when the author's experience is drawn upon and illustrative cases are aptly quoted.

While space is not afforded for much detail in this book-notice, a few interesting topics may be chosen and commented upon. Paracentesis thoracis is carefully described and the dangers are pointed out. Under the author's discussion of "syncope" occurring while inducing artificial pneumothorax it is suggested that oxygen is preferable to air, as oxygen seems less likely to induce symptoms from the side of the nervous system. Whether or not this is borne out in practice and by experiment is of much interest. Regarding serum therapy in pneumonia we quote the author's opinion that "the Felton concentrated serum is the best yet produced." The chapters on disease of the circulatory system are well written, and the discussions of the use of digitalis, of oxygen and of venesection contain much of worth-while information for students and practitioners of medicine.

The criticism made when the third edition was under review is still applicable, we think—possibly too much space has been given to the description and diagnosis of disease, while on the other hand perhaps too brief discussion has been given to certain agents used in treatment, *e.g.*, water, light, etc. As the third edition was better than the second, so the fourth is much better than the third. It is therefore strongly recommended to the students and practitioners.

Treatment in General Practice. Harry Beckman, M.D., Professor of Pharmacology, Marquette University School of Medicine, Milwaukee, Wisc. Second edition, revised; 889 pages. Price $11.50. W. B. Saunders, London and Philadephia; McAinsh & Co., Toronto, 1934.

The first edition of this ambitious work was reviewed in the *Journal* four years ago. This second edition has been greatly improved by a new format. From cover to cover there are many evidences that a painstakingly thorough revision has been made; besides, many new subjects not presented in the first edition have been added and the book has been brought well up to date. The author's personal opinion is more frequently noted than in the former edition which gives an added value.

As a single volume text-book on the therapeutics of medical diseases, the author has set for himself a very high standard, which he has successfully attained. He shows a well-balanced judgment in his advice, and is moreover cautious in advising methods which are not of proved value. There are few of the diseases met with in temperate or in torrid zones which are not considered in this volume. Of interest are the historical summaries of many of the major subjects considered. For the numerous references to the diseases under discussion there is an extensive bibliography which shows the thoroughness with which the author has completed a worthwhile task. This book can be most heartily recommended.

The Modern Treatment of Syphilis. Joseph E. Moore, M.D., Associate in Medicine, Johns Hopkins University, etc. 535 pages. Price $5.00. Chas. C. Thomas, Springfield and Baltimore, 1933.

This book should be in the hands of every medical practitioner treating syphilis who is not satisfied with a mere perfunctory and usually inadequate routine sufficient only to quell active symptoms. Every phase of the therapeutic attack on this disease is dealt with thoroughly and rationally. The author is well-known as head of the Syphilis Division of the Medical Clinic of Johns Hopkins Hospital.

The first chapter on the Biology of Syphilitic Infection is of great importance for the basis of the structure which follows. The questions of latency, biological "cure", clinical arrest, re-infection and superinfection are handled lucidly. The correlation of clinical facts with experimentally derived data is a constant aim. Another chapter of elemental importance is that on the Appraisal of the Therapeutic Problem in the Patient. Those who have followed with attention the literature of anti-syphilitic therapy will observe that little of note has appeared which does not receive due and critical consideration.

Many departures from rather commonly accepted views and practices will strike the reader. While he is in agreement with very many prominent syphilologists in giving emphatic preference to arsphenamin over neoarsphenamin in early syphilis, the author pointedly differs from Schamberg in insisting upon high dosage. He compromises with Harrison on the question of the combined intermittent treatment preferred by the latter to alternating (arsenic and heavy metal) continuous treatment, in recommending combined treatment during the first few doses in early syphilis, but after that, alternating. Beyond that he is an uncompromising advocate of continuous treatment, rather than interrupted, giving a minimum of 20 arsenical injections in the first seven or eight months. In latent and late benign syphilis neoarsphenamin is preferred, 20 injections being the mini-

mum requirement. In Moore's clinic bismuth has almost replaced mercury in late as well as early syphilis.

The author, after seven years' experience with sodium thiosulphate, has seen no evidence that it is of any value, either in arsphenamin dermatitis or any other type of arsenical or heavy metal intoxication, and for a year has abandoned it as worthless. On the other hand he has gained the impression that calcium gluconate is of some value, thus supporting the observation and practice of several other workers, although it is astonishing to find him using it intravenously, in view of the cases of fatal thrombosis which have been reported following its use by this route.

In view of the "disgraceful state of chaos" referred to as existing with regard to the preparations of bismuth now offered, the chapter on bismuth is of particular value. What little is known, or for the acceptance of which there is believed to be adequate evidence, is clearly and logically set down. Moore considers that its treponemastatic action chiefly commends it, wherein he differs from Stokes and others who speak of its "resistance-building" effect. His preference, for which he gives impressive reasons, is for the insoluble preparations, especially the salicylate.

Special chapters deal respectively with the treatment of cardio-vascular syphilis, visceral syphilis, ocular syphilis, neurosyphilis and congenital syphilis in an exceptionally thorough, not to say exhaustive, manner.

This work is one of the most valuable contributions that has been made to the literature of syphilis in recent years, and is unhesitatingly commended as a practical guide and work of reference.

Hypertension and Nephritis. Arthur M. Fishberg, Associate Physician to Beth Israel Hospital. Third edition. 668 pages, illustrated. Price $6.50. Lea & Febiger, Phila., 1934.

The present volume is the third edition of a book which needs little introduction to the medical profession, as the first two editions have already received well merited recognition. In this, the third, edition extensive changes have been necessitated by recent progress in the field of arteriolar and renal physio-pathology. The therapeutic use of magnesium sulphate, the treatment of mercury poisoning, the kidney in multiple myeloma, the injection of acacia in œdema, arteriolar necrosis in hypertension, and the nature and treatment of renal and hypertensive disease in pregnancy are only a few of the subjects which have been thoroughly revised and brought up to date. In spite of a complete review of the literature dealing with the subject, and particularly the question of the physiology of renal and cardio-vascular disease, the author has succeeded in escaping involved discussions of a theoretical nature. On the other hand, he has predigested all of the information, therapeutic and diagnostic, that practice, clinic, and laboratory have revealed, and has presented the best of it in simple practical terms, which should make the book unusually attractive to the general practitioner. Not the least interesting section is that devoted to dietetic measures. Emphasis has been laid upon dietaries suitable for home treatment rather than upon the more elaborate methods for special institutions. The book is heartily recommended alike to the specialist and general practitioner.

Rose and Carless' Manual of Surgery. Cecil P. G. Wakeley, D.Sc., F.R.C.S., F.R.S., and John B. Hunter, M.C., M.C.(Canatab.), F.R.C.S., Surgeons, King's College Hospital. Fourteenth edition, 1,487 pages, illustrated. Price $8.50. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1933.

This is the fourteenth edition of the most popular text-book in English, one which has also been translated into three foreign languages. There can be nothing but praise for the changes that have been made in this new volume — the insertion of new material, the compression of the text, and the new illustrations. The general character of the book has been definitely changed by the delegation of several chapters to different writers. The volume can no longer be looked upon as a summary of the personal teachings of the editors, but as a compilation of the opinions of a group of British surgeons. The popularity of the work on this side of the Atlantic would probably be enhanced by a judicious policy of deletion of material which is undoubtedly accurate and was at one time important, but not at the moment interesting or pertinent for the modern student. It may be said that the work will probably hold its place as the standard text-book for undergraduates.

Practice of Surgery. Russell Howard, C.B.E., M.S., F.R.C.S., Surgeon, London Hospital, and Alan Perry, M.S., F.R.C.S., Surgeon, London Hospital. Fourth ed., 1,338 pages, illustrated. Price $9.00. Ed. Arnold & Co., London; Macmillan Co., Toronto, 1933.

The new edition of this work, by the well known London teacher of surgery, Russell Howard, assisted by Allan Perry, lives up to the well-earned reputation of its predecessors. The text is written in a clear, concise style, is easy to read, and the subject matter well chosen. Much that is unnecessary to the student is omitted, and rarely what is necessary.

The preface states that the aim of the author is to create a text-book for students. Bearing this in mind, the subject is presented chiefly from a diagnostic and treatment point of view. The recommendations are, for the most part, those recognized and practised in surgery to-day. These are placed before the reader in sound and at times dogmatic statements. One cannot always agree with the author, particularly when he says that compound fissured fractures of the skull should be trephined, in anticipation of lesions. Lumbar puncture is not mentioned in the treatment of head injuries, nor is mention made of some of the well recognized applications of sympathetic ganglionectomy. The index would be improved by more cross-indexing. Bone tumours are not dealt with under the most recent classification, and one misses the term "osteogenic sarcoma", both in the index and text. This book should have a definite appeal to students, and will no doubt be read by many.

Fractures. Paul B. Magnuson, M.D., Associate Professor of Surgery, Northwestern Medical School, Chicago. 466 pages, illustrated. Price $6.00. J. B. Lippincott, Phila., London and Montreal, 1933.

This new work by Magnuson, of Chicago, has much to commend it. Written by a surgeon who with his many other qualifications is a member of the Fracture Committee of the American College of Surgeons, he has herein embodied the results of his many years' experience in the treatment of fractures in an entirely satisfactory way. The first four chapters deal with "fundamentals," the pathology and repair of fractures, the mechanics of displacement, and the equipment necessary in handling fractures.

Throughout the volume it is noted that the author has endeavoured to simplify methods of treatment. Special emphasis is placed on the value of sound anatomical and physiological knowledge in approaching the problem of fractures. Only those methods of treatment have been included which in his hands have been most successful. In case of fracture of the clavicle, as might be expected, he condemns the old-time Sayre's dressing, "because of its constricting pull on the upper arm and pressure on the elbow. The results are not so satisfactory as with the use of the clavicular cross." In the treatment of supracondylar fracture of the humerus, of the neck of the femur, and of the patella, the author's methods, with which he has had good results, are described. Operative methods of treatment are given due consideration. What lends much attractiveness to this treatise is the clear succinct way in which

the author expresses his opinions, even though they may appear on occasion to be somewhat dogmatic. As a modern up-to-date exposition on the care and treatment of fractures, this book can be heartily recommended.

Diseases of Infants and Children. J. P. Crozer Griffith, M.D., Ph.D., Emeritus Prof. of Pædiatrics, University of Pennsylvania, and A. Graeme Mitchell, M.D., B.K., Rachford Prof. of Pædiatrics, University of Cincinnati. 1,155 pages, illustrated. Price $11.50. W. B. Saunders, London and Phila.; McAinsh & Co., Toronto, 1933.

This is a one volume edition of Griffith and Mitchell's two volume text-book. The reviewer, not being intimately acquainted with the previous editions, is not in a position to make comparisons between the old and the new, but it seems to him that the authors set themselves an impossible task. This was "to maintain the text-book as a work of reference for pædiatric practitioners and writers, and at the same time fit it for the needs of undergraduate students". To this reviewer the first requirement of a text-book for undergraduate students is simplicity, directness and clarity of statement. A certain degree of dogmatism is necessary. The great text-books bear the imprint of the mind and manner of their author. Their greatness depends not upon facts contained but upon the manner of their presentation. There is no heart-throb but only lifeless profusion of statement behind such a sequence as the following:— (p. 824): "When the total blood-protein falls below 5.5 per cent or the albumin below 2.5 per cent, œdema is usually present (Moore and Van Slyke[81]). Œdema, while paralleling these findings, changes more rapidly than do the alterations in the blood-protein (Calvin and Goldberg[82]). The increase in blood-fat so often present also helps in maintaining the osmotic pressure (Fishberg[83]). The blood chlorides are increased during periods of œdema. Doubly refractile lipoid bodies are found in the urine by means of polarizing microscope, as first described by Munk[70]".

The authors have succeeded in obscuring their own personalities at the same time throwing in the retina of the reader's mind a rapidly changing jumble of flashing colours. The results are not happy. One wonders what such omnivorous readers think, but one has no way of telling. A student or a general practitioner would find the book exhausting. For the pædiatric practitioner or writer it is perhaps more useful on account of the many references given. These must total up in the thousands. But one would suggest they might be as readily presented without distracting the reader's mind were proper names omitted from the text. Thus for example, (p. 698) the statement "Tuberculosis is an unusual cause of chronic laryngitis in early life, especially in infancy and early childhood, although reported by Barthez and Sanne,[3] Rheindorff,[4] Heubner,[5] and Demme,[6]", could be more concisely stated, "Tuberculosis is an unusual cause of chronic laryngitis in early life,[3, 4, 5, 6]". Further, the references at the end of each chapter would be easier to use were large type used for the text reference numbers rather than the journal volume numbers. This book will be more useful as a source book in a reference library than elsewhere.

The Injured Workman. G. F. Walker, M.D., M.R.C.P., and collaborators. 190 pages. Price $1.75. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1933.

By far, the greater number of Workmen's Compensation cases are clear-cut and definite in their history. The injury is, without doubt, the result of an accident arising out of or in the course of employment, and surgical treatment brings the case to a close with either complete recovery, or some definite disability, such as the loss of a limb or the stiffness of a joint. In a not inconsiderable number of cases, however, disturbing factors enter into the picture. Strange disabilities, often with only subjective manifestations, make their appearance unexpectedly after minor accidents. The vexed question of aggravation of existing disease arises, and finally, sometimes, we meet the out-and-out malingerer.

It is to the general practitioner dealing with his occasional case in the second category that "The Injured Workman" is addressed. The first chapter is a concise summary of the British Workmen's Compensation Act and an explanation of the meaning of its provision as interpreted by court decision. This chapter is written by Mr. J. Harvey Robson, Barrister-at-Law. The main portion of the book was written by Doctor Walker, and may be divided into two parts. The first (Chapter III) considers, in order, special injuries to various parts of the body and points out the possible and probable sequelæ to each of these accidents. The second part (Chapter IV) aids our reasoning in reverse order, and, taking certain diseases, such as cancer, tuberculosis, pneumonia and heart disease, points out the possibility of traumatic causation or aggravation. Space does not, of course, permit of a full discussion of all the points made, but the serviceableness of the book is enhanced rather than diminished by its index-like form. A particularly valuable feature is the section on "rusting" and "brooding".

Consideration of injuries of the ear, nose and throat, is left to Dr. R. E. Jowett, in a subsequent chapter, and Dr. John Foster has written an interesting section on injuries to the eyes, including a full discussion of sympathetic ophthalmia.

Recent Advances in Sex and Reproductive Physiology. J. M. Robson, M.D., B.Sc., F.R.S.E., Beit Memorial Research Fellow, Institute of Animal Genetics, University of Edinburgh. 249 pages, illustrated. Price 12/ 6d. J. & A. Churchill, London, 1934.

The title of this recent addition to a valuable series is misleading, in that the field actually covered is rather small. The book deals, in fact, with experimental studies on the parts played by ovarian and hypophyseal hormones in reproductive processes in female mammals, covering much the same ground as the well-known monographs by Parkes and Zondek. Knowledge is advancing so rapidly in this field that books rapidly become out of date, and, indeed, the present volume gives a rather disappointing impression of having been written some eighteen months ago, with a few later additions; it is, for instance, decidedly less up-to-date than Cameron's "Recent Advances in Endocrinology," published some months ago. Within its own field and its own period, however, this work presents a well-organized and lucid review of carefully selected papers from the enormous literature. A valuable feature is that special attention is paid to experimental work on monkeys, and the concluding chapter deals briefly with clinical applications of the new knowledge. The illustrations deserve a word of praise.

Laboratory Medicine. A Guide for Students and Practitioners. Daniel Nicholson, M.D., Assistant Professor of Pathology, University of Manitoba. Second edition, 566 pages, illustrated. Price $6.50. Lea & Febiger, Phila., 1934.

This second edition of Nicholson's well known book on laboratory medicine is a worthy successor to his first complete, but yet brief and concise, work. It covers a multitude of subjects ranging from laboratory equipment to the treatment of anæmia. In the present edition many new clinical and laboratory procedures are outlined. These include the cough plate method for the diagnosis of whooping-cough, pneumococcus typing by the rapid capsular reaction, Carper's simple method for culturing the tubercle bacillus in sputum, and the urea-clearance test for renal function. Many other procedures have been revised and improved. Not the least valuable part of the work, particularly from the view-point of the practitioner, is the interpretation of the results of laboratory procedures. The chapters dealing with the classification of anæmias, immunity tests, and immunization in diphtheria and scarlet fever, convalescent sera in poliomyelitis, measles, mumps and whooping cough are unusually interesting. The book is highly recommended to both student and practitioner.